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IN ENGLISH TRANSLATION



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ENTHALPY OF MIXING IN THE SODIUM – TIN SYSTEM

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In the present communication we present the results of measuring the electromotive force (EMF) of the concentration cell Na electrolyte with Na^+ ions Na + Sn (I) over a wide range of temperatures (400-650°) and sodium concentrations in the alloy. The data obtained was used for calculating the enthalpy of mixing of liquid alloys of sodium and tin at 600°.

The activity of sodium in liquid alloys with tin was first determined by the EMF method by Hauffe and Vierk [1] at 480° over the concentration range of 0.467-0.950 atom fraction of sodium (N_{Na}). Later, in connection with the use of a tin-sodium glass electrode, this system was studied by Yu. K. Delimarskii and A. A. Kolotii [2] for alloys with N_{Na} = 0.25-0.88. Subsequently A. F. Alabyshev and A. G. Morachevskii [3, 4] investigated the thermodynamic properties of this system over a wide range of compositions at 475-575°. However, the experimental data presented in the works listed did not allow the calculation of the enthalpy of mixing over the whole range of compositions since they did not give reliable information on the temperature coefficient of the EMF $\left(\frac{dE}{dT}\right)$ over the concentration range N_{Na} = 0.35-0.75. It seemed interesting to calculate the value of the enthalpy of mixing from EMF measurements over a wide temperature range and to compare the values obtained with the results available in the literature on direct calorimetric measurements of the enthalpy of mixing of this system, carried out by McKisson and Bromley [5]. With this aim, we again measured the EMF of cell (I) over the temperature range given above and for sodium concentrations from 0.05 to 0.85 atom fraction.

MEASUREMENT PROCEDURE

The measurement procedure used in the present work was mainly analogous to that described previously [1, 3, 6]. The electrolyte used was the heat-resistant glass "Durabax", containing 2.0% of Na_2O. The measurements were made in an atmosphere of carefully purified argon. For the work we used high-purity metals (Kahlbaum analytical-grade tin and sodium).

MEASUREMENT RESULTS AND THEIR DISCUSSION

Fig. 1 shows the temperature dependence of the EMF for alloys of various compositions. As the figure shows, a linear dependence of EMF on temperature was observed for all the alloys investigated.

Table 1 gives the values of the EMF (E), the temperature coefficient of the EMF $\left(\frac{dE}{dT}\right)$ and also values calculated from the usual relations [7] for the partial molar isobaric-isothermal potentials ($\Delta\bar{Z}_{Na}$) and enthalpies of mixing ($\Delta\bar{H}_{Na}$) of sodium at 600°. Fig. 2 gives the relation of $\frac{dE}{dT}$ to alloy composition. This figure also shows the temperature coefficients of the EMF from paper [2]. In the region of compositions rich in sodium ($N_{Na} > 0.76$) $\frac{dE}{dT}$ was positive. In the region of metallic compound formation the temperature coefficient was negative, but for alloys with $N_{Na} < 0.15$ it was again positive. The extreme value of $\frac{dE}{dT}$ lay in the composition

TABLE 1

Values of the EMF, Temperature Coefficient of the EMF and Partial Molar Isobaric Potential and Enthalpy of Mixing of Sodium (600°)

N_{Na}	E (in V)	$\frac{dE}{dT} \cdot 10^4$ (V/deg)	$\overline{\Delta Z}_{Na}$	$\overline{\Delta H}_{Na}$
0.05	0.5130	1.0	—11830	—9820
0.10	0.4553	0.32	—10500	—9860
0.15	0.4222	—0.05	— 9740	—9830
0.21	0.3722	—0.53	— 8700	—9740
0.25	0.3678	—0.50	— 8480	—9490
0.29	0.3410	—0.88	— 7865	—9640
0.40	0.2821	—1 20	— 6500	—8920
0.50	0.2130	—0.96	— 4900	—6840
0.60	0.1307	—0.46	— 3020	—3940
0.70	0.0672	—0.30	— 1550	—2150
0.80	0.0278	0.15	— 640	— 340

TABLE 2

Enthalpies in the Sodium – Tin System

Composition	ΔH (in kcal/g-at)	Temperature (in °C)	Source
$NaSn_2$	—5.0	298°	[10,11]
	—6.7	298	[11,13]
	—3.65 ± 0.25	880	[5]
	—3.25	873	Our data
NaSn	—5.5	298	[10,11]
	—8.0	298	[11,13]
	—6.0	298	[14,15]
	—4.8 ± 0.14	882	[5]
	—4.55	873	Our data
$Na_{1.105}Sn$	—4.86 ± 0.04	881	[5]
Na_4Sn_3	—5.1	298	[10,11]
	—8.0	298	[11,13]
	—4.65 ± 0.3	880	[5]
	—4.70	873	Our data
Na_2Sn	—4.0	298	[10,11]
	—7.0	298	[11,13]
	—4.8	298	[14,15]
	—4.03 ± 0.08	885	[5]
	—4.4	873	Our data
Na_4Sn	—4.2	298	[10,11]
	—6.8	298	[11,13]
	—2.9	298	[14,15]
	—2.5 ± 0.5	880	[5]
	—3.15	873	Our data

region corresponding to the compound NaSn, which is the most stable compound in this system (congruent melting point equal to 576°). A similar composition dependence of the value $\frac{dE}{dT}$ was also observed for other sodium alloys characterized by metallic compound formation, in particular, the sodium-cadmium and sodium-lead systems [3]. Fig. 2 shows that for a series of compositions our data agree satisfactorily with the data of [2], but these data referring to the range of medium compositions, N_{Na} = 0.5-0.7, seem incorrect to us. The presence of two minima on the "$\frac{dE}{dT}$ – composition" curve seems doubtful to us.

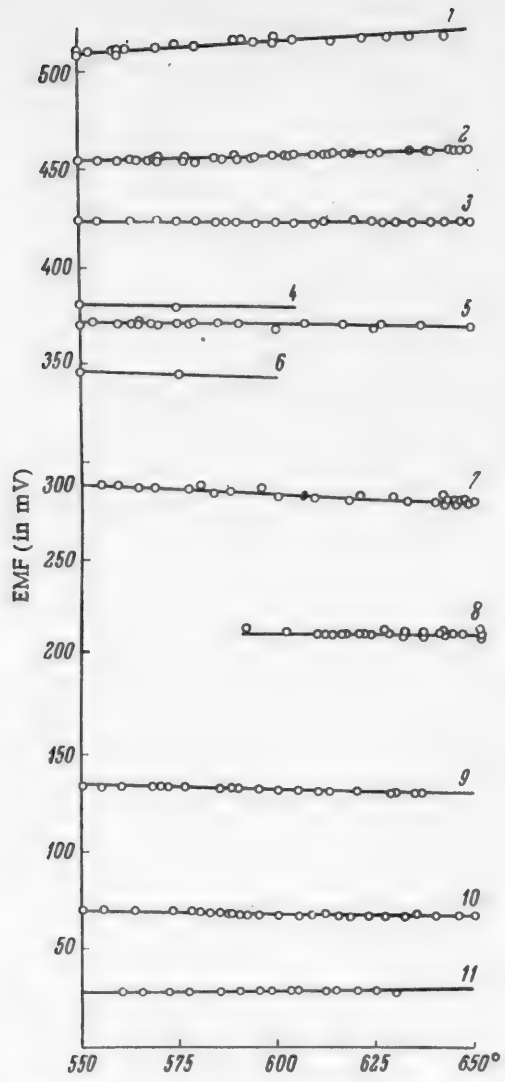


Fig. 1. Temperature dependence of the EMF of the cell Na|glass|Na-Sn for alloys of various composition. N_{Na}: 1) 0.05, 2) 0.10, 3) 0.15, 4) 0.21, 5) 0.25, 6) 0.29, 7) 0.40, 8) 0.50, 9) 0.60, 10) 0.70, 11) 0.80.

Fig. 3 gives the curves of partial molar enthalpy of mixing of the components and the corresponding integral curve. The extreme value of ΔH lay at $N_{Na} = 0.57$.

Fig. 4 compares the integral thermodynamic characteristics of the sodium-tin system with the phase diagram of this system [8]. The integral curves of the enthalpy of mixing and also the isobaric ΔZ and excess isobaric ΔZ^X potentials have extremes close to the composition corresponding to the compound NaSn. The maximum values were as follows: $\Delta H = -4700$ cal/g-at., $\Delta Z = -3940$ cal/g-at. Fig. 4 shows that ΔH was mainly determined by the value of the isobaric potential. The value of the entropy component of $T\Delta S$ was small. In the region of compound formation $T\Delta S$ had a negative value. The figure also shows that ΔH did not equal ΔZ^X. In our case the maximum values of ΔH and ΔZ^X differed by 1900 cal. This indicated that the Na-Sn system is not a "regular" one [9] and that despite [2], even in the first approximation the value of $\Delta \bar{H}_{Na}$ cannot be identified with the value $RT\ln\gamma_{Na}$ (γ_{Na} is the activity coefficient of sodium in the alloy).

Table 2 gives the enthalpies of mixing of the liquid alloys for compositions corresponding to compounds formed in the Na-Sn system, according to our data and according to the data of McKisson and Bromley [5, 12]. For comparison, Table 2 also gives the enthalpies of formation of solid alloys in the Na-Sn system according to the data of various authors.

As data in Table 2 show, the values we obtained for the enthalpies of mixing agree quite satisfactorily with the results of direct calorimetric measurement [5]. According to our data, the maximum of the integral ΔH curve is somewhat displaced from the composition of the most stable compound in the system (NaSn) towards the region of compositions rich in sodium. This is apparently connected with the fact that in a liquid alloy of sodium with tin, together with structural groups of the compound NaSn there also exist structural groups of the congruently melting compound Na_2Sn. The maximum of the integral ΔZ curve (Fig. 4) was also displaced toward the sodium-rich composition region. Similar displacements in the maxima of the integral curves were also observed in the sodium – lead system [16]. Only if the system had one congruently melting compound would the maxima of the ΔH, ΔZ and ΔZ^X integral curves correspond to the composition of this compound [3, 16].

Some displacement in the maximum of the ΔH curve for alloys of sodium with tin was also observed in the work of McKisson and Bromley (Table 2).

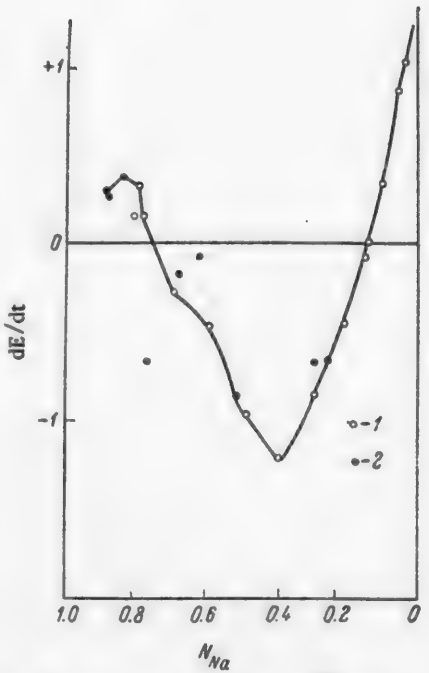


Fig. 2. Relation of the value $\frac{dE}{dT}$ (V/deg.) to alloy composition. 1) Our data, 2) data of [2].

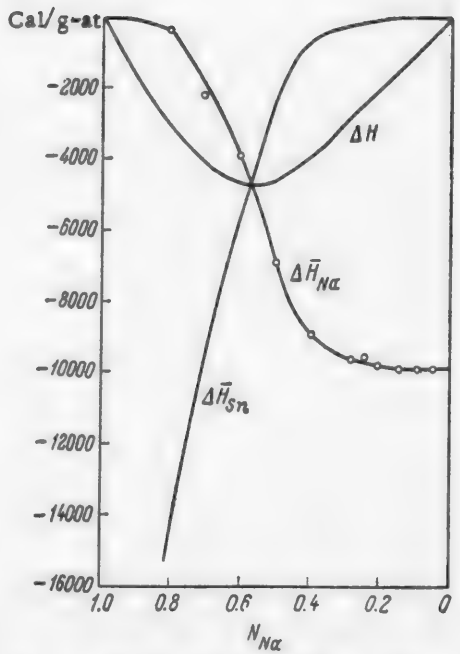


Fig. 3. Enthalpy of mixing in the Na-Sn system at 600°.

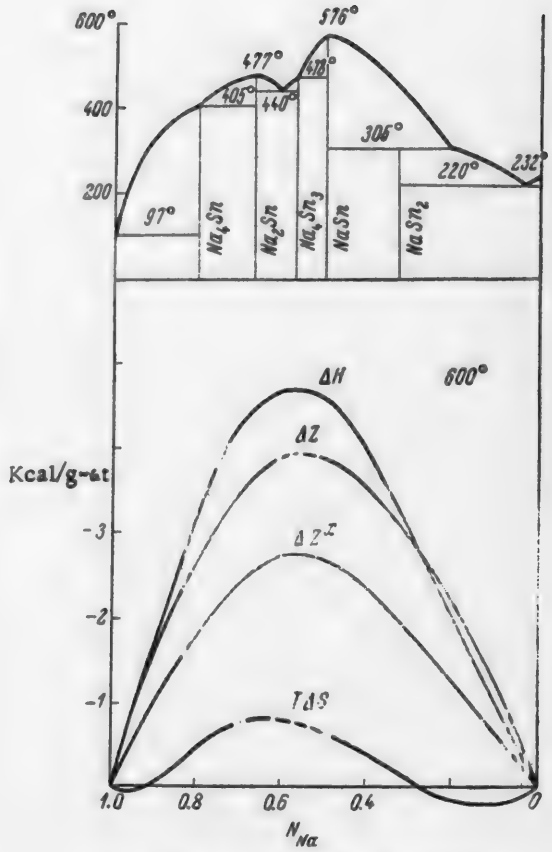


Fig. 4. ΔH, ΔZ, ΔZ^X and TΔS for the Na-Sn system at 600° and the phase diagram of the system.

SUMMARY

1. Measurements were made of the EMF of the concentration cells sodium|glass|sodium – tin alloy at 400-650° over a wide range of compositions.

2. The enthalpies of mixing in the Na-Sn system at 600° were calculated. The results obtained were compared with the data from direct calorimetric measurements.

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FORMATION OF PENTATHIONATES BY THE ACTION OF ACIDS ON THIOSULFATES IN THE PRESENCE OF SALTS OF CERTAIN ORGANIC BASES

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A large number of works have been devoted to investigating the formation of polythionic acids and, in particular, pentathionic acid by the acidification of thiosulfate solutions. Certain authors [1-3] consider that free thiosulfuric acid partially condenses into pentathionic acid by the over-all equation

$$5H_2S_2O_3 = 2H_2S_5O_6 + 3H_2O \quad (1)$$

In this case the yields of pentathionic acid are extremely low and purifying it from other polythionic acids formed simultaneously presents considerable difficulties. There are papers [4-7] where various mechanisms have been proposed for the formation of pentathionic acid through a series of hypothetical intermediate compounds. An interesting fact is the sharp increase in the yield of pentathionic acid to 80-90% on acidification of thiosulfate in the presence of arsenous acid, which acts as a catalyst. This reaction was discovered by Salzer [3] and studied by other authors [2, 5-8].

In one of their recent works, R. K. Eremenko and A. I. Brodskii [8] wrote that "the role of arsenite apparently consists of the transfer of a sulfide sulfur atom from one molecule of thiosulfate to two others with the formation of pentathionate:"

$$[As] + S_2O_3^{--} = [As]S + SO_3^{--},$$
$$[As]S + 2S_2O_3^{--} = [As] + S_5O_6^{--},$$

where [As]S is the intermediate sulfide compound formed from arsenite and thiosulfate.

The presence of many theories put forward for explaining the reactions occurring during the acidification of thiosulfate solutions or in Wackenroder's solution indicates that at present there is no satisfactory explanation of the mechanism of pentathionic acid formation in the cases described above.

We studied the decomposition of thiosulfuric acid in the presence of salts of diethyldecyl-, diethyldodecyl-, tributyl-*, triisoamyl,* trihexyl-*, triheptyl-, tri-n-decyl-, octadecyl, methyloctadecyl- and diethyl-β-phenoxyethylamines and also trimethyldecyl-, dimethylisoamyldecyl-, dimethylisoamyldodecyl- and dimethylisoamylbenzylammonium salts. The presence of tributylamine, diethyl-β-phenoxyethylamine and dimethylisoamylbenzylammonium salts had no noticeable effect on the reaction and we only observed the normal decomposition of thiosulfuric acid with the liberation of sulfur. In the presence of the rest of the salts of organic bases investigated, the main reaction product was pentathionic acid, which could be isolated as the salt with the organic base.

*Synthesized by O. E. Morozova.

Name of substance	Structural formula	Empirical formula	Sulfur content (in %)		n_D^{20}
			calc.	found	
Diethyldecylamine penthationate	$\left[C_{10}H_{21}-N\begin{matrix}C_2H_5\\C_2H_5\end{matrix}\right]_2 \cdot H_2S_5O_6$	$C_{28}H_{64}O_6N_2S_5$	23.42	23.74	1.5110
Triisoamylamine pentathionate	$[iso\text{-}C_5H_{11})_3N]_2 \cdot H_2S_5O_6$	$C_{30}H_{68}O_6N_2S_5$	22.48	22.79	1.5040
Diethyldodecylamine pentathionate	$\left[C_{12}H_{25}-N\begin{matrix}C_2H_5\\C_2H_5\end{matrix}\right]_2 \cdot H_2S_5O_6$	$C_{32}H_{72}O_6N_2S_5$	21.63	21.46	1.5050
Dimethylisoamyldecylammonium pentathionate	$\left[\begin{matrix}C_{10}H_{21}\\iso\text{-}C_5H_{11}\end{matrix}N\begin{matrix}CH_3\\CH_3\end{matrix}\right]_2 S_5O_6$	$C_{34}H_{76}O_6N_2S_5$	20.84	20.85	1.5090
Tri-n-hexylamine pentathionate	$[(C_6H_{13})_3N]_2 \cdot H_2S_5O_6$	$C_{36}H_{80}O_6N_2S_5$	20.11	20.0	—
Dimethylisoamyldodecylammonium pentathionate	$\left[\begin{matrix}C_{12}H_{25}\\iso\text{-}C_5H_{11}\end{matrix}N\begin{matrix}CH_3\\CH_3\end{matrix}\right]_2 S_5O_6$	$C_{38}H_{84}O_6N_2S_5$	19.43	19.86	1.5095
Tri-n-heptylamine pentathionate	$[(C_7H_{15})_3N]_2 \cdot H_2S_5O_6$	$C_{42}H_{88}O_6N_2S_5$	18.30	18.10	1.4960
Tri-n-decylamine pentathionate	$[(C_{10}H_{21})_3N]_2 \cdot H_2S_5O_6$	$C_{60}H_{124}O_6N_2S_5$	14.14	14.22	1.4900

The formation of pentathionic acid proceeded in aqueous or aqueous alcohol solution at room temperature immediately after acidification of a mixture of solutions of thiosulfate and the salt of the organic base and gave yields close to quantitative. It was established that the sulfur liberated on acidification of an aqueous or aqueous alcohol solution of thiosulfate redissolved when the salt of a quaternary ammonium base was added. In this case pentathionic acid was isolated from the solution and identified in the form of the salt with the corresponding quaternary ammonium base. The solution of sulfur was accompanied by the liberation of hydrogen sulfide, indicated by the blackening of lead acetate added to the reaction solution.*

In the absence of the salts of organic bases, the evolution of hydrogen sulfide was not observed and the precipitate of lead salts remained colorless.

The disappearance of colloidal sulfur from an acidified thiosulfate solution cannot be explained simply by its solution in the presence of the surface-active ammonium salt since it was shown that colloidal sulfur in a bicarbonate medium did not dissolve on addition of an ammonium salt. On the basis of the experiments we arrived at the conclusion that the formation of pentathionic acid on acidification of thiosulfate in the presence of the salts of certain amines and quaternary ammonium bases proceeded mainly according to the following equations:

$$2H_2S_2O_3 \longrightarrow 2H_2SO_3 + 2S \longrightarrow 2H_2SO_3 + S_2, \qquad (2)$$

$$2H_2S_2O_3 + S_2 \xrightarrow[\text{base}]{\text{salt of organic}} H_2S_5O_6 + H_2S. \qquad (3)$$

Hydrogen sulfide liberated by reaction (3) immediately reacted with the sulfur dioxide formed by decomposition of thiosulfuric acid; this again liberated sulfur and the whole process was repeated from the beginning until the thiosulfuric acid was completely converted into pentathionic acid according to the over-all equation (1).** Reaction (3) has not been described in the literature. It should be noted that colloidal sulfur (S_β), liberated

*At definite quantitative ratios of the components (a large amount of thiosulfate and a small amount of acid) hydrogen sulfide could also be detected by odor and by the blackening of lead acetate paper placed over the reaction solution. In control experiments without ammonium salts hardly any evolution of hydrogen sulfide occurred.

**According to [9], hydrogen sulfide reacts with $H_2S_2O_3$ according to the equation $3H_2S_2O_3 + H_2S = H_2S_6O_6 + S + 3H_2O$. However, we did not detect the presence of hexathionic acid.

from an acetone solution with water, did not react with the formation of pentathionic acid in the presence of sulfurous acid and a dimethylisoamyldecylammonium salt.

All the pentathionates obtained in this work were viscous liquids with a yellowish tinge. They had no odor and were insoluble in water, benzene, ether or ligroin, but partially dissolved these substances; they were readily miscible with methyl and ethyl alcohols and acetone; alkali solution decomposed them to organic base, sulfur and thiosulfate, which is characteristic of pentathionates [10].

We did not determine the specific gravities of the pentathionates as their high viscosity made this very difficult.

The table gives the names, analytical results* and refractive indices for pentathionates which have not been described in the literature. Trimethyldecyl- and trimethyldodecylammonium pentathionates and also the pentathionates of octadecyl- and methyloctadecylamines were not isolated in a sufficiently pure form due to purification difficulties. The procedure for obtaining pentathionates is described in the experimental section for two examples; in the first one, the readily water-soluble dimethylisoamyldecylammonium salt was used and in the second, the water-insoluble hydrochloride of tri-n-decylamine. Experiments on the basis of reaction (3) were carried out similarly.

EXPERIMENTAL

1. Preparation of Dimethylisoamyldecylammonium Pentathionate. A solution of 2.91 g of dimethylisoamyldecylammonium chloride (0.01 mole) in 20 ml of water was mixed with a solution of 3.7 g of $Na_2S_2O_3 \cdot 5H_2O$ (0.015 mole) in 30 ml of water and then acidified with 6 ml of dilute (1:4) hydrochloric acid. An oily liquid separated 2-3 seconds after acidification. The reaction mixture was allowed to stand for a few hours and then the upper aqueous layer carefully decanted and the lower oily layer dissolved in a few milliliters of ethanol. The solution was filtered and the solvent removed in vacuum by heating on a glycerol bath (bath temperature 80-85°). For complete removal of the solvent and traces of water, the substance was kept under the given conditions (80-85°, 2 mm Hg) for 30 minutes. We obtained 3.8 g of a viscous, yellowish oil. Its yield was close to quantitative. The sulfur content was 20.4% and indicated the quite high degree of purity of the product.

3.5 g of the unpurified dimethylisoamyldecylammonium pentathionate was dissolved in 5 ml of ethanol and precipitated by the addition of 12 ml of distilled water to the solution. The upper aqueous layer was decanted, 2 ml of ethanol added to the residual oil and the substance again precipitated with 5 ml of water. The oily layer which separated was dissolved in 3-4 ml of ethanol, filtered, the alcohol removed and the product dehydrated under the conditions given above. We obtained 3.1 g of extremely pure dimethylisoamyldecylammonium pentathionate as a yellow, viscous oil with $n^{20}D$ 1.5090.

Found %: C 53.03; H 10.02; N 3.65; S 20.82. $C_{34}H_{76}O_6N_2S_5$. Calculated %: C 53.08; H 9.96; N 3.64; S 20.84.

2. Preparation of Tri-n-decylamine Pentathionate. 4.38 g of tri-n-decylamine (0.01 mole) was dissolved in a mixture of 150 ml of methanol and 5 ml of dilute (1:4) hydrochloric acid and the solution of tri-n-decylamine hydrochloride obtained was mixed with a solution of 3.7 g of $Na_2S_2O_3 \cdot 5H_2O$ (0.015 mole) in 10 ml of water and acidified with 2 ml of concentrated hydrochloric acid. Five minutes after acidification, 50 ml of water was added to the clear solution. An oily layer separated and this was allowed to stand for a few hours. The upper aqueous methanol layer was carefully removed and the lower one dissolved in 20 ml of methanol, filtered to remove a small amount of sulfur and precipitated with 4 ml of distilled water. The product was reprecipitated twice and then dissolved in 10 ml of methanol and the solution kept at room temperature for 30 minutes. At this, an extremely small amount of excess sulfur precipitated. The solution was filtered and the methanol removed in vacuum by heating on a glycerol bath (80-85°) and the residual substance heated in vacuum for 30 minutes. We obtained 4.4 g of tri-n-decylamine pentathionate. The yield of purified substance was about 77 weight % of theoretical, which is explained by losses during purification.

The substance was a yellowish, viscous oil with $n^{20}D$ 1.4900.

Found %: S 14.22. $C_{60}H_{128}O_6N_2S_5$. Calculated %: S 14.14.

*The analyses were carried out in the Institute of Petrochemical Synthesis, Acad. Sci. USSR.

3. Interaction of Sulfur With Thiosulfuric Acid in the Presence of Quaternary Ammonium Salts. a) Reaction in the presence of dimethylisoamyldodecylammonium bromide in an aqueous medium. 15 g of $Na_2S_2O_3 \cdot 5H_2O$ was dissolved in 50 ml of water, acidified with 8 ml of dilute (1:2) hydrochloric acid and the solution quickly divided into half. One minute after acidification, to one half of the solution was added excess sodium bicarbonate solution (blank experiment) and to the other, a solution of 7.3 g of dimethylisoamyldodecylammonium bromide (0.02 mole) in 20 ml of water. Both solutions were shaken for 2-3 minutes. In the blank experiment, the precipitated sulfur collected in lumps; 0.21 g of it was obtained. In the solution containing the quaternary ammonium salt, the sulfur that precipitated initially disappeared almost completely (only 0.04 g of sulfur remained); here the separation of an oily layer was observed. It was reprecipitated three times from an alcohol solution with water, washed with ether, dissolved in ethanol and filtered and the solvent removed as indicated above. We obtained 3.0 g of dimethylisoamyldodecylammonium pentathionate, which corresponds approximately to the amount of sulfur which reacted; $n^{20}D$ 1.5083.

Found %: C 55.28; H 10.30; N 3.41; S 19.70. $C_{38}H_{81}O_6N_2S_5$. Calculated %: C 55.29; H 10.26; N 3.39; S 19.43.

b) Reaction in the presence of dimethylisoamyldodecylammonium bromide in an aqueous alcohol medium. 1.24 g of $Na_2S_2O_3 \cdot 5H_2O$ was dissolved in 25 ml of water, 20 ml of ethanol added and the solution acidified with 2 ml of dilute (1:4) hydrochloric acid. Colloidal sulfur precipitated and the solution became opaque. Five minutes after acidification it was treated with 20 ml of 0.5 M dimethylisoamyldodecylammonium bromide solution and shaken periodically for three minutes. The sulfur dissolved completely and the solution became quite clear.

c) Reaction in the presence of dimethylisoamyldecylammonium chloride in an aqueous medium. 10 g of $Na_2S_2O_3 \cdot 5H_2O$ was dissolved in 40 ml of water and acidified with 4 ml of dilute (1:4) hydrochloric acid and the solution quickly divided into two. One minute after acidification, one half of the solution was neutralized with sodium bicarbonate and to both halves were added 10 ml portions of 1.0 M aqueous solution of dimethylisoamyldecylammonium chloride. The flasks with the two solutions were closed with stoppers on which were fixed strips of filter paper, moistened with lead acetate solution. With the bicarbonate neutralized solution, neither solution of the sulfur nor blackening of the lead acetate paper was observed. Rapid and complete solution of the sulfur in the acid solution was observed. Simultaneously hydrogen sulfide was liberated and this was detected both by odor and by blackening of the lead acetate paper. Dilution of this solution with water liberated an oily layer, which settled over quite a long period. The usual purification yielded 0.3 g of a viscous, yellowish oil with $n^{20}D$ 1.5090 and containing 20.4% of sulfur, which corresponds to dimethylisoamyldecylammonium pentathionate. The blank experiment without the quaternary ammonium salt showed that hardly any hydrogen sulfide was liberated on acidification of thiosulfate under the chosen conditions.

d) Effect of nature of organic base on formation of pentathionic acid. 7.4 g of $Na_2S_2O_3 \cdot 5H_2O$ was dissolved in a few milliliters of water, acidified with 1 ml of dilute (1:4) hydrochloric acid and the solution quickly divided into three equal portions. The solution rapidly became turbid due to the liberation of colloidal sulfur. One minute after the acidification, to portion I was added 2 ml of 0.5 M dimethylisoamyldecylammonium chloride solution, to portion II, 2 ml of 0.5 M dimethylisoamylbenzylammonium chloride solution and the solutions shaken for several hours.

In the first case the sulfur dissolved and an oily layer was formed, while in the second, no visible changes occurred.

Immediately after shaking, 1.5 ml portions of saturated lead acetate solution were added to all three solutions. In solution I, which contained the dimethylisoamyldecylammonium salt, the solution immediately acquired a brown color, while in solutions II and III, the precipitates of lead salts and the solutions themselves were practically colorless. Fifteen minutes after the addition of lead acetate, solution I had become completely black, while the other two solutions had only an extremely weak coloration.

SUMMARY

1. The decomposition of thiosulfuric acid in the presence of salts of certain higher amines and quaternary ammonium bases was studied.

2. It was shown that in the presence of the salts of a series of symmetrical tertiary amines from $(iso\text{-}C_5H_{11})_3N$

to $(C_{10}H_{21})_3N$ and diethylalkylamines, where the alkyl contains 10 or 12 carbon atoms, and also salts of quaternary ammonium bases, dimethylisoamyldecyl- and dimethylisoamyldodecylammonium salts, the decomposition of thiosulfates with acids leads to the formation of pentathionates of the corresponding organic bases in yields close to quantitative.

3. An explanation was put forward for the formation of pentathionic acid from thiosulfuric acid, that an S_2 molecule, formed by partial decomposition of thiosulfuric acid in the presence of salts of certain organic bases, reacts with thiosulfuric acid.

4. We prepared and characterized 8 previously undescribed neutral pentathionates, namely the pentathionates of triisoamyl-, tri-n-hexyl-, tri-n-heptyl-, tri-n-decyl-, diethyldecyl- and diethyldodecylamines and also dimethylisoamyldecyl- and dimethylisoamyldodecylammonium pentathionates.

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PHYSICOCHEMICAL INVESTIGATION OF THE INTERACTION OF ZIRCONIUM HALIDES WITH ESTERS OF MONOBASIC ACIDS

V. COMPLEXES OF ZIRCONIUM IODIDE

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In our previous communications [1-4] we presented the results of investigating the interaction of zirconium tetrachloride and tetrabromide with esters of monobasic carboxylic acids. It was established that replacement of the chlorine in the zirconium tetrahalide by bromine did not have a great effect on the polarity of complexes with the composition $ZrHal_4 \cdot E$, while going from the chloride to the bromide, complexes with the composition $ZrHal_4 \cdot 2E$ were dissociated much more strongly in benzene (with the exception of the complex with ethyl formate) and even after suppression of the dissociation by excess ester, the polarity of the complexes with zirconium bromide remained considerably lower than in the case of the chloride. It was shown that the complexes of $ZrCl_4$ and $ZrBr_4$ with esters with the composition $ZrHal_4 \cdot 2E$ dissociated in benzene according to the scheme $ZrHal_4 \cdot 2E \rightleftharpoons ZrHal_4 \cdot E + E$; no appreciable dissociation of complexes with the composition $ZrHal_4 \cdot E$ into components was detected. It was also established that the alcohol residue of the ester had hardly any effect on the polarity of complexes with $ZrCl_4$, but on going to $ZrBr_4$, there was a noticeable effect with the polarity of the complexes increasing with an increase in this residue.

It was interesting to follow how the properties of zirconium halide complexes with esters would change on going from zirconium bromide to iodide. There is much less literature data [5] on the polar properties of complexes of metal iodides with organic addends. The polar properties of iodides of group IV metals with organic addends have not been investigated at all (with the exception of the dipole moments of titanium, zirconium and tin iodides in dioxane [6]).

In the present work we present the results of studying the polar properties of zirconium iodide complexes with esters of monobasic carboxylic acids in benzene.

The procedures for the dielectrometric investigations and purification of the reagents used in the work were given previously [1, 6, 7]. The starting benzene solutions of the complexes were prepared by dissolving zirconium iodide in benzene containing an amount of ester corresponding strictly to the amount of iodide taken. All the solutions had a red color and fumed strongly in air. During their preparation and investigation, precautions were taken to prevent their contact with atmospheric moisture.

Table 1 gives the results of measuring the dielectric permeability (ϵ) and density (d) and the calculated values of the molecular polarization of the complex $ZrI_4 \cdot CH_3COOC_2H_5$ in benzene. These data show that within the limits of experimental error, the complex $ZrI_4 \cdot CH_3COOC_2H_5$ has a dipole moment equal to that of the analogous complex with zirconium bromide [4]. The curve of the polarization of this complex against concentration indicates its slight tendency for association (much less than for the analogous complexes of zirconium chloride and bromide) and the absence of noticeable dissociation into components.

Tables 2-6 give data on the molecular polarization of the complexes $ZrI_4 \cdot 2HCOOC_2H_5$, $ZrI_4 \cdot 2CH_3COOC_2H_5$, $ZrI_4 \cdot 2CH_3COOC_3H_7$, $ZrI_4 \cdot 2\text{-i-}CH_3COOC_4H_9$ and $ZrI_4 \cdot 2C_3H_7COOC_2H_5$ in benzene. The character of the concentration dependence of the polarization of the complex $ZrI_4 \cdot 2HCOOC_2H_5$ (a fall in polarization with dilution)

TABLE 1

Complex $ZrI_4 \cdot CH_3COOC_2H_5$ in benzene
(P_∞ = 320 cm³, R = 96.3 cm³, μ = 3.17 D)

c	ε_{20}	d_4^{20}	P cm³
0.00331	2.342	0.8964	296
0.00266	2.332	0.8928	299
0.00195	2.322	0.8890	308
0.00157	2.315	0.8869	306

TABLE 2

Complex $ZrI_4 \cdot 2HCOOC_2H_5$ in benzene
(P_∞ = 500 cm³, R = 110.1 cm³, μ = 4.24 D)

c	ε_{20}	d_4^{20}	P cm³
0.00794	2.890	0.9201	1073
0.00528	2.660	0.9065	1039
0.00384	2.545	0.8990	1009
0.00292	2.471	0.8940	962
0.00209	2.402	0.8896	855

TABLE 3

Complex $ZrI_4 \cdot 2CH_3COOC_2H_5$ in benzene
(P_∞ = 390 cm³, R = 118.6 cm³, μ = 3.49 D)

c	ε_{20}	d_4^{20}	P cm³
0.00617	2.419	0.9122	396
0.00409	2.369	0.9007	376
0.00308	2.350	0.8952	379
0.00233	2.335	0.8911	379
0.00179	2.325	0.8882	383

TABLE 4

Complex $ZrI_4 \cdot 2CH_3COOC_3H_7$ in benzene
(P_∞ = 460 cm³, R = 121.6 cm³, μ = 3.93 D)

c	ε_{20}	d_4^{20}	P cm³
0.00547	2.418	0.9075	446
0.00384	2.375	0.8989	430
0.00288	2.353	0.8939	438
0.00226	2.341	0.8906	436
0.00177	2.331	0.8879	447

TABLE 5

Complex $ZrI_4 \cdot$ 2-i-$CH_3COOC_4H_9$ in benzene
(P_∞ = 530 cm³, R = 137.1 cm³, μ = 4.23 D)

c	ε_{20}	d_4^{20}	P cm³
0.00570	2.454	0.9086	530
0.00374	2.391	0.8983	509
0.00289	2.368	0.8938	510
0.00253	2.359	0.8919	514
0.00187	2.341	0.8884	516

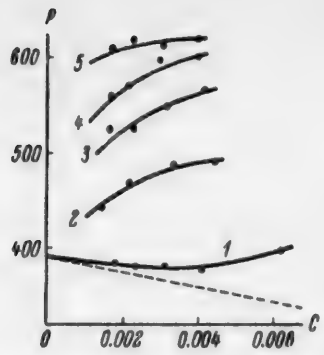
TABLE 6

Complex $ZrI_4 \cdot 2C_3H_7COOC_2H_5$ in benzene
(P_∞ = 354 cm³, R = 137.2 cm³, μ = 3.07 D)

c	ε_{20}	d_4^{20}	P cm³
0.00499	2.371	0.9046	358
0.00352	2.348	0.8975	357
0.00259	2.332	0.8926	353
0.00206	2.324	0.8897	357
0.00161	2.316	0.8872	354

indicates the dissociation of this complex. The complexes $ZrCl_4 \cdot 2HCOOC_2H_5$ and $ZrBr_4 \cdot 2HCOOC_2H_5$ which we studied previously [1, 4] had less tendency for dissociation (they only showed appreciable dissociation at concentrations below 0.003 mole fraction). On going to zirconium iodide, the complex with ethyl formate dissociated appreciably even at much higher concentrations.

The concentration dependences of the molecular polarization of complexes formed by zirconium iodide with ethyl acetate, propyl acetate and isobutyl acetate (Tables 3-5) have the same character: Withan increase in concentration the polarization first falls somewhat and then begins to increase. A similarly complex concentration dependence of the polarization was also observed for the complex $ZrBr_4 \cdot 2C_3H_7COOC_2H_5$ [4]. Apparently at very low concentrations the second ester molecule is practically completely eliminated and the fall in polarization with a concentration increase is caused by association of the complex with the composition $ZrI_4 \cdot E$. With a further increase in concentration, the fraction of more polar complex molecules with the composition $ZrI_4 \cdot 2E$ increases and the polarization begins to grow. The polarization of the complex $ZrI_4 \cdot C_3H_7COOC_2H_5$ (Table 6) hardly changes with concentration. Evidently at concentrations below 0.005 mole fraction, with this molecule the second ester molecule is practically completely eliminated.



Polarization of the ZrI_4 complex with ethyl acetate in benzene. Molecular ratio of ZrI_4 to ethyl acetate; 1) 1 : 2, 2) 1 : 4, 3) 1 : 6, 4) 1 : 8, 5) 1 : 12.

That the value of P_∞, obtained from data presented in Tables 2-5, corresponds to the polarization of the complexes $ZrI_4 \cdot E$, i.e. to complete elimination of the second ester molecule, is indicated by the following fact. The difference in the value of P_∞ for the complexes $ZrI_4 \cdot CH_3COOC_2H_5$ and $ZrI_4 \cdot 2CH_3COOC_2H_5$ (Tables 1 and 3) is 70 cm^3. In a previous paper [3] we noted that the difference in the value P_∞ for complexes $ZrHal_4 \cdot E$ and $ZrHal_4 \cdot 2E$, with the condition that at $c \to 0$ one ester molecule is completely eliminated from the second complex, must be equal to the difference in the polarization of the ester in benzene and that of benzene itself. This difference is 67 cm^3 for ethyl acetate. Thus, analysis of the concentration dependence curves of the polarization leads to the conclusion that for complexes of ZrI_4 with esters of monobasic acids, as for complexes of $ZrCl_4$ and $ZrBr_4$, with an increase in the acid radical (formate, acetate and butyrate) the stability of the bond with the second ester molecule decreases.

Table 7 and the figure show data on the molecular polarizations of the ZrI_4 complex with ethyl acetate in benzene at various molecular ratios of zirconium iodide and ethyl acetate.

The letter c_1 and c_2 denote the concentrations of the complex $ZrI_4 \cdot 2CH_3COOC_2H_5$ and of excess ethyl acetate, expressed in mole fractions. The calculation of the polarization was based on the composition of the complex $ZrI_4 \cdot 2CH_3COOC_2H_5$, i.e., it was assumed that zirconium iodide reacted with only two molecules of ester.* The polarization of the free ethyl acetate, i.e., the excess over that required for formation of the complex $ZrI_4 \cdot 2CH_3COOC_2H_5$, was taken as equal to 94 cm^3. From the total molecular polarization of the solution we subtracted the value 94 c_2, i.e., the contribution to the polarization from the excess ethyl acetate.

By graphical interpolation of the data from Tables 3 and 7 we obtained the values of the molecular polarization of the complex $ZrI_4 \cdot 2CH_3COOC_2H_5$ at a concentration of 0.00200 mole fraction with various excesses of ethyl acetate ($P_{0.00\text{ }2}$). Extrapolation of these values to an infinitely great excess of ethyl acetate gave $P_{compl.} = 650$. We consider this value the approximate value of the molecular polarization of the undissociated complex $ZrI_4 \cdot 2CH_3COOC_2H_5$. It corresponds to a dipole moment $\mu = 4.97$ D.

Assuming that in the absence of interaction with the second molecule of ethyl acetate, the polarization of the ZrI_4 complex with ethyl acetate would change with an increase in concentration in the direction indicated by a dotted line on the figure (i.e., in the same way that the polarization of the complex $ZrI_4 \cdot CH_3COOC_2H_5$ changes, Table 1), we calculated the degree of dissociation (α) and the dissociation constant (K) of the complex by the formulas

$$\alpha = \frac{P_{compl.} - P_c}{P_{compl.} - P_\infty} \qquad K = \frac{\alpha^2 c}{1 - \alpha},$$

where P_∞ is the polarization of the complex with complete elimination of one molecule (dotted line on the figure); P_C is the polarization at the given concentration of the complex $ZrI_4 \cdot 2CH_3COOC_2H_5$; $\underline{c}$ is the molar concentration of the complex.

For solutions 1 and 3, Table 3, we obtained $\alpha_1 = 0.81$, $\alpha_3 = 0.94$, $K_1 = 2.3 \cdot 10^{-1}$, $K_3 = 5.0 \cdot 10^{-1}$, $K_{av} = 3.5 \cdot 10^{-1}$.

For the complexes $ZrCl_4 \cdot 2CH_3COOC_2H_5$ and $ZrBr_4 \cdot 2CH_3COOC_2H_5$ we previously [3, 4] obtained values of the dissociation constants of the order of $2 \cdot 10^{-4}$ and $2 \cdot 10^{-2}$, respectively. Thus, in the series zirconium chloride – bromide – iodide an increase is observed in the dissociation of the complexes $ZrHal_4 \cdot 2CH_3COOC_2H_5$ by the scheme $ZrHal_4 \cdot 2E \rightleftharpoons ZrHal_4 \cdot E + E$.

*We showed previously [3] that zirconium chloride reacts with not more than two molecules of ester. In the series zirconium chloride – bromide – iodide, the bond even with the second ester molecule decreases regularly. Therefore the interaction of zirconium iodide with more than two molecules of ester is improbable.

TABLE 7

Complex of ZrI_4 With Ethyl Acetate in Benzene With Various Excesses of Ethyl Acetate

c_1	c_2	ε_{2_1}	d_4^{20}	P cm³
a) Molecular ratio of ZrI_4 to ethyl acetate 1 : 4 ($P_{0.002} = 462$ cm³)				
0.00441	0.00882	2.448	0.9006	491
0.00332	0.00664	2.407	0.8951	487
0.00214	0.00428	2.362	0.8892	468
0.00142	0.00284	2.335	0.8856	441
b) Molecular ratio of ZrI_4 to ethyl acetate 1 : 6 ($P_{0.002} = 527$ cm³)				
0.00411	0.01644	2.498	0.8991	566
0.00309	0.01236	2.441	0.8940	548
0.00222	0.00888	2.394	0.8897	525
0.00161	0.00644	2.365	0.8866	524
c) Molecular ratio of ZrI_4 to ethyl acetate 1 : 8 ($P_{0.002} = 568$ cm³)				
0.00393	0.02358	2.536	0.8982	599
0.00295	0.01770	2.472	0.8933	596
0.00210	0.01260	2.414	0.8890	569
0.00165	0.00990	2.386	0.8868	559
d) Molecular ratio of ZrI_4 to ethyl acetate 1 : 12 ($P_{0.002} = 610$ cm³)				
0.00395	0.0395	2.625	0.8999	618
0.00302	0.0302	2.540	0.8950	610
0.00221	0.0221	2.472	0.8905	616
0.00167	0.0167	2.425	0.8874	608

A comparison of the concentration dependence curves of the molecular polarization for complexes with other esters leads to the conclusion that this rule is characteristic of all the complexes $ZrHal_4 \cdot 2E$ studied. This rule may be formulated as a decrease in the tendency to form complexes with the coordination number 6. A coordination number of 5, corresponding to complexes with the composition $ZrHal_4 \cdot E$, is much more characteristic of zirconium iodide than of zirconium chloride.

To show this rule in the change in polarity of the complexes studied in the series zirconium chloride – bromide – iodide is more difficult. Dissociation of the complexes $ZrHal_4 \cdot 2E$ lowers the apparent polarity of the complexes, which makes it difficult to compare the values of their dipole moments. Therefore, we limited ourselves to comparing the dipole moments of the complexes $ZrHal_4 \cdot E$, which are not dissociated in solution, and also of the complexes $ZrHal_4 \cdot 2CH_3COOC_2H_5$, whose dipole moments were obtained by suppressing the dissociation with excess ester. In addition, it is possible to compare the dipole moments of the complexes $ZrCl_4 \cdot 2HCOOC_2H_5$ and $ZrBr_4 \cdot 2HCOOC_2H_5$ since they hardly dissociate, and also of the complexes $ZrHal_4 \cdot 2C_3H_7COOC_2H_5$, since they dissociate completely to $ZrHal_4 \cdot C_3H_7COOC_2H_5$.

For complexes with the composition $ZrHal_4 \cdot CH_3COOC_2H_5$ in the series zirconium chloride – bromide – iodide we have the dipole moments 3.89 D, 3.15 D and 3.17 D, i.e., a fall in going from chloride to bromide and a very small increase, within the limits of experimental error, in going from bromide to iodide. An analogous rule was observed for complexes with the composition $ZrHal_4 \cdot 2CH_3COOC_2H_5$ (after suppression of dissociation with excess ethyl acetate), which had dipole moments of 7.13, 4.50 and 4.97 D. For complexes with ethyl formate, the transition from chloride to bromide produced a slight increase in polarity: 7.65 and 7.85 D for the complexes $ZrHal_4 \cdot 2HCOOC_2H_5$ and 4.15 and 4.50 D for the complexes $ZrHal_4 \cdot HCOOC_2H_5$. The polarity of complexes with the composition $ZrHal_4 \cdot C_3H_7COOC_2H_5$ hardly changed in the series zirconium chloride – bromide. The complexes $ZrHal_4 \cdot 2C_3H_7COOC_2H_5$ had the dipole moments 5.23, 3.80 and 3.07 D in the series zirconium

chloride – bromide – iodide. Let us add to this that the dipole moments of zirconium halides in dioxane [6, 8] have the values 5.94 D for $ZrCl_4$, 4.68 D for $ZrBr_4$ and 5.3 D for ZrI_4.

The data presented indicate that the change in polarity of the complexes in the series zirconium chloride – bromide – iodide has a complex character. In going from zirconium chloride to bromide and from bromide to iodide, no definite rule was observed in the change in the polarity of the complexes. In general, on going from zirconium chloride to iodide the polarity of the complexes decreases.

Comparison of the data on the polarity of the complexes $ZrHal_4 \cdot E$ and $ZrHal_4 \cdot 2E$ leads to the conclusion that all the complexes with the composition $ZrHal_4 \cdot 2E$ studied have a cis- structure.

Data on the molecular polarization of the complexes $ZrI_4 \cdot 2CH_3COOC_2H_5$, $ZrI_4 \cdot 2CH_3COOC_3H_7$ and $ZrI_4 \cdot$ 2-i-$CH_3COOC_4H_9$ (Tables 3-5) indicates an increase in the polarity of the complexes with an increase in the length of the alcohol radical of the ester. An analogous rule was observed previously [4] for complexes of zirconium bromide with acetates, while for complexes of zirconium chloride with acetates, the alcohol radical had no noticeable effect on the polarity of the complexes [1]. It is possible that this rule is caused by dispersion interaction of the alcohol residue with the halide. In the series chlorine – bromine – iodine, the polarizability of the halogen increases and this may lead to an increase in the dispersion interaction.

SUMMARY

1. We measured the dipole moments of the complexes $ZrI_4 \cdot CH_3COOC_2H_5$, $ZrI_4 \cdot 2HCOOC_2H_5$, $ZrI_4 \cdot 2CH_3COOC_2H_5$, $ZrI_4 \cdot 2CH_3COOC_3H_7$, $ZrI_4 \cdot$ 2-i-$CH_3COOC_4H_9$ and $ZrI_4 \cdot 2C_3H_7COOC_2H_5$ in benzene.

2. It was established that an increase in the acid radical of the ester led to a decrease and an increase in the alcohol radical led to an increase in the polarity of the complexes studied.

3. By means of the dielectric permeability, we determined the approximate value of the dissociation constant of the complex $ZrI_4 \cdot 2CH_3COOC_2H_5$.

4. For complexes of zirconium tetrahalides with esters of monobasic acids, in the series zirconium chloride – bromide – iodide an increase was observed in the tendency of complexes with the composition $ZrHal_4 \cdot 2E$ to dissociate (elimination of the second ester molecule), a decrease in the tendency of complexes with the composition $ZrHal_4 \cdot E$ to associate and a growth in the effect of the alcohol radical (toward increasing the polarity of the complexes).

5. With an increase in the acid radical, the tendency of the complexes with the composition $ZrHal_4 \cdot 2E$ to dissociate increased.

6. No definite rule was observed for the change in polarity of the complexes in going from zirconium chloride to bromide and from bromide to iodide. The change from zirconium chloride to iodide led to a decrease in polarity.

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INVESTIGATION IN THE FIELD OF VAPOR-PHASE CATALYTIC HYDRATION OF ACETYLENE AND ITS DERIVATIVES

V. EFFECT OF THE ANIONS OF SOLID CATALYSTS

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According to the ideas presented in previous communications [1, 2], the activation of acetylene during its vapor-phase hydration into acetaldehyde under the effect of catalysts, namely phosphoric acid salts, is only achieved when the cations of these salts are metals characterized by a certain structure in the external layers of the electron sheath (Cu, Cd, Zn).* The question arose as to what was the effect of the anion in the salt used as a catalyst. M. G. Kucherov [3] showed that the hydration of acetylene and its derivatives in the liquid phase could occur under the effect of various mercury salts, namely the bromide, sulfate, chloride and acetate. In the patent literature, one finds information on the possibility of using not only sulfuric, but also phosphoric and acetic acids [4]. Travagli [5] observed that the rate of acetylene absorption depended on the nature of the acid. R. M. Flid et al. [6] consider that the catalytic activity of acid solutions of mercury salts depends only on the value of the oxidation potential of these solutions. M. R. Lozovskii and S. M. Mendeleva [7] hydrated acetylene over various solid mercury salts, namely the phosphate, molybdate and vanadate. In patents, the sulfides, selenides, chromates, tungstates and molybdates of cadmium and zinc [8], neutral and acid orthophosphates or metaphosphates of cadmium [9], cadmium and zinc oxides and also tungsten and molybdenum trioxide and vanadium pentoxide [10] have been proposed for the vapor-phase process.

In order to study the effect of anions, we investigated the cadmium and calcium salts of various acids. Cadmium was chosen as an active cation and calcium as an inactive cation [2], which would not mask the catalytic properties of anions. We studied simultaneously the effects of some of these anions on catalysts of an acid nature, on free acids, phosphoric and tungstic, and on anhydrides, molybdic and vanadic. We should note that we could only use those acids or anhydrides, which were quite stable and nonvolatile at high temperatures. Phosphoric acid was deposited on activated charcoal and the other substances were tested without carrier. Table 1 gives the results of studying the catalytic activity of two series of salts and some of the acids corresponding to them. For comparison we give data on the catalytic activity of cadmium and calcium hydroxides (oxides) as compounds which do not contain acid anions. All the catalysts were tested at the same temperature, and equal acetylene volume rates and water-vapor dilutions were used. The experiments differed only in duration.

The data obtained show that cadmium tungstate and phosphates were most active. In selectivity of action, the cadmium salts differed considerably: on the tungstate, molybdate and silicate, quite considerable amounts of acetic acid were obtained together with acetaldehyde, while the vanadate caused the formation of only acetic acid and acetone. The yields of crotonaldehyde also varied. Cadmium hydroxide occupied a special position. On the one hand, it had a low over-all activity and on the other, it catalyzed the formation of acetone more than formation of acetaldehyde. Under the conditions of the process, there was considerable reduction of the cadmium hydroxide to metallic cadmium (a metal film appeared on the walls of the reaction tube). In the case of cadmium salts, very small traces of metal were noticed only on spent molybdate and vanadate. Calcium salts were found to be practically inactive (the somewhat different behavior of calcium tungstate will be discussed below). Catalysts of an acid nature were considerably more effective. It is interesting to note that here

*Mercury also has a similar structure, but its salts were shown to be active only in liquid-phase hydration.

TABLE 1

Composition of catalyst		Test duration (in hours)	Extent of C_2H_2 conversion (in %)	Yield of reaction products on C_2H_2 converted (in mole %)			
cation	anion			CH_3CHO	crotonaldehyde	CH_3COOH	acetone
Cd	Orthophosphate	9	71.3	77.0	9.4	0.7	1.0
	Pyrophosphate	4	81.8	79.9	11.4	1.5	Not determined
	Tungstate	9	89.4	74.5	6.8	14.9	The same
	Molybdate	9	64.9	72.4	Not determined	14.3	3.0
	Vanadate	9	61.0	0.0	0.0	7.1	93.1
	Silicate	9	56.9	63.7	6.2	13.4	8.9
	Hydroxide	4	22.6	26.8	0.0	16.2	59.9
Ca*	Orthophosphate	2.5	3.3	—	—	—	—
	Pyrophosphate	2.5	3.5	—	—	—	—
	Tungstate	2.5	15.1	—	—	—	—
	Hydroxide	3.0	0.8	—	—	—	—
H	Orthophosphate	15	30.9	76.1	Not determined		
	Tungstate	30	32.2	74.1	The same		
	Molybdate	4	11.8	64.6	Not determined	24.1	Traces
	Vanadate	4	16.8	29.6	The same	28.3	4.0

*Due to the low extent of acetylene conversion on calcium salts, the reaction products were not analyzed. The presence of aldehyde in them was confirmed qualitatively.

TABLE 2

Composition of salt	Specific surface of freshly prepared samples (m^2/g)	Duration of catalyst operation (in hours)	Specific surface of spent samples (m^2/g)
Neutral orthophosphate	13.2	40	9.1
		170	9.0
Tungstate	—	43	16.5
Pyrophosphate	12.4	580	10.1
Silicate	—	10	92.4
Molybdate	—	25	12.1
Hydroxide	—	10	7.7

tungstic and phosphoric acids also had a higher activity, though only the former could operate steadily for a long period, while on phosphoric acid the degree of acetylene conversion fell continuously from experiment to experiment and the pyro- and meta-acids were formed [11] and were gradually removed from the catalyst zone with the reaction products.

We determined the specific surface of some cadmium salts by low temperature adsorption of nitrogen by the BET method [12]. The data obtained are presented in Table 2. Of these salts, cadmium silicate was distinguished by its great specific surface (apparently it contained a certain amount of free SiO_2). During the vapor-phase hydration of acetylene we observed some decrease in the specific surface of the catalysts, occurring as a result of the prolonged action of high temperature (390-400°).

The specific catalytic activity at 50% acetylene conversion was calculated for cadmium orthophosphate, pyrophosphate and tungstate [13]. By a series of experiments with samples of the same catalyst with different grain sizes (from 0.75 to 3.0 mm), it was first established that with a grain size of 3 mm the reaction proceeded

TABLE 3

Composition of catalyst	$K \cdot 10^3$
Neutral orthophosphate	3.2
Pyrophosphate	3.4
Tungstate	2.1

in the kinetic region. The specific activities of the two phosphates and the tungstate were found to be of the same order (Table 3).

The effect of the anion of solid catalysts, namely various salts whose cation was cadmium, could determined by the extent of the ionic state of the lattice, i.e., the value of the cation charge. Since all these salts were apparently ionic crystals, the effect of the anion on the activation of acetylene and the formation of a polar complex with the cation [1, 2] was not appreciable in going from one salt to another.

As regards cadmium oxide, the bonds in its lattice have an intermediate character in between ionic and covalent [14], and consequently the charge on a cation in it must be less than in salts. This may be the reason why cadmium oxide has a lower catalytic activity than salts of this metal.

The data presented above indicate that the nature of the cation mainly affects secondary processes, as a result of which the aldehyde is partially converted into side products. In connection with this, in our schemes presented in [1, 2] the basic primary acts of the process are accomplished only by participation of the cation of the catalysts and the anion is not involved in them.

It was noted above that cadmium hydroxide (oxide) catalyzed to a considerable extent the conversion of acetylene into acetic acid and acetone. The formation of the same substances on a series of cadmium salts (tungstate, molybdate and vanadate) also indicates that the latter undergo partial thermal dissociation [15] with the formation of a certain amount of CdO and the corresponding acidic oxide; we also cannot exclude the possibility of partial hydrolysis of the salt by water vapor with the liberation of $Cd(OH)_2$, which is converted into CdO. The most selective catalysts and consequently those with the least tendency for dissociation or hydrolysis and the most stable cadmium salts must be considered the orthophosphate and the pyrophosphate. The formation of crotonaldehyde was the result of the greater or lesser condensing capacity of the catalyst with respect to acetaldehyde.

The insignificant activity of most of the calcium salts was caused by the incapacity of the calcium ion to act on the acetylene. The higher activity of calcium tungstate may be explained by thermal dissociation or hydrolysis proceeding on the surface of the catalyst with the formation of calcium oxide or tungsten oxide (or tungstic acid); since the former is inactive (see Table 1), apparently, in this case tungstic acid must act as the catalyst. Since the anion does not play a major role in the hydration process, the considerable activity of catalysts of the acid type which do not contain an acetylene activating cation (see Table 1) may be explained by the catalytic action of the hydrogen ion (proton). It may be supposed that when the catalysts used are not acids themselves, but their anhydrides, the addition of water occurs in the surface layers of the catalyst with the formation of acids and their dissociation to ions.

$$MoO_3 + H_2O \rightleftarrows H_2MoO_4 \rightleftarrows 2H^{\cdot} + MoO_4''$$

According to data in [16], a proton adds directly to an acetylene molecule with the formation of a carbenium ion, which then reacts with water. In view of the extremely great affinity of a proton for water [17], we consider that a proton may also interact with water molecules adsorbed on the catalyst, forming a hydroxonium ion. The latter then adds to acetylene with the formation of vinyl alcohol, which then isomerizes to acetaldehyde:

$$CH \equiv CH + (H_3O)^+ \longrightarrow (CH_2{=}CH{-}OH_2)^+ \longrightarrow CH_2{=}CHOH + H^+ \longrightarrow CH_3CHO$$

The high yields of acetic acid on molybdic and vanadic anhydrides indicate the capacity of the latter to produce the oxidation of acetaldehyde. However, the yields of acetone on them were insignificant in comparison with the corresponding cadmium salts, since in the absence of CdO, acetic acid does not undergo further conversions.

EXPERIMENTAL

As acetylene hydration catalysts we used chemically pure tungstic acid, molybdic and vanadic anhydrides and calcium hydroxide. They were compressed into tablets before use. Phosphoric acid was deposited onto AR-3 activated charcoal, purified by boiling with dilute nitric acid, washing with water and drying. The content of 100% phosphoric acid was 45% of the weight of the catalyst. The other catalysts were prepared by precipitation. Neutral cadmium orthophosphate was precipitated by the action of triammonium phosphate on a solution of cadmium nitrate. The molar ratio of $CdO : P_2O_5$ found was 2.96 and that calculated for $Cd_3(PO_4)_2$ was 3.0. Neutral calcium orthophosphate was precipitated by the action of triammonium phosphate on calcium nitrate solution. The molar ratio of $CaO : P_2O_5$ found was 2.95 and that calculated for $Ca_3(PO_4)_2$ was 3.0. Cadmium pyrophosphate was obtained by the dissociation at 400° of cadmium ammonium phosphate, obtained by precipitation from cadmium nitrate with diammonium phosphate. The molar ratio of $CdO : P_2O_5$ found was 1.95 and that calculated for $Cd_2P_2O_7$ was 2.0. Calcium pyrophosphate was obtained by dissociation at 400° of acid calcium orthophosphate, precipitated from calcium nitrate by diammonium phosphate. The molar ratio of $CaO : P_2O_5$ found was 2.01 and that calculated for $Ca_2P_2O_7$ was 2.0. Cadmium tungstate was obtained by Jander's method [18]. Tungstic acid was dissolved in 10% ammonia by heating and the excess ammonia was neutralized with acetic acid. To the neutralized solution was added a solution of cadmium nitrate. The percentage cadmium found was 30.6 and that calculated for $CdWO_4$ was 31.2. Calcium tungstate was precipitated similarly to cadmium tungstate. The percentage calcium found was 14.3 and that calculated for $CaWO_4$ was 13.9. Cadmium molybdate was precipitated by the action of ammonium molybdate solution on cadmium acetate solution at 60°. The percentage Cd found was 41.2 and that calculated for $CdMoO_4$ was 41.3. Cadmium vanadate was precipitated by the action of ammonium vanadate solution on cadmium acetate solution at 60°. The percentage of Cd found was 36.5 and that calculated for $Cd(VO_3)_2$ was 36.2. Cadmium silicate was precipitated from cadmium acetate solution by treatment with sodium silicate to complete precipitation. The percentage Cd found was 60.1 and that calculated for $CdSiO_3$ was 59.6. Cadmium hydroxide was precipitated by the method of Vollenius [19] from a boiling cadmium nitrate solution by the addition of the stoichiometric amount of sodium hydroxide solution.

The catalysts were washed with water, dried and compressed into tablets. The P_2O_5, Cd and Ca contents of them were determined by the usual gravimetric and volumetric methods [20]. The phosphoric acid was precipitated with ammonium molybdate and determined by a volumetric method; cadmium was isolated as the sulfide and then converted into the sulfate and calcium was precipitated as the oxalate, which was determined by the permanganate method.

The apparatus and experimental procedure for the hydration of acetylene were described previously [2]. Into the reaction tube was loaded 50 ml of catalyst. The experiments were carried out at 390-400°, an acetylene volume rate of 150 liters/liter of cat./hour and the acetylene diluted with water in a ratio of 1:10 (in moles). The duration of the experiments was 3-5 hours. Regeneration of catalyst between experiments on the same catalyst was not carried out. Table 1 gives average data from several experiments.

The reaction products were analyzed for the acetaldehyde, crotonaldehyde, acetic acid and acetone contents. The total content of carbonyl compounds in the aqueous condensate was determined with hydroxylamine hydrochloride. The crotonaldehyde content was determined by bromination of the double bond. Acetone was determined by Messinger's method [21] through iodoform; aldehydes present were first removed by oxidation with silver oxide. The amount of acetaldehyde was calculated from the total carbonyl compound content by subtraction of acetone and crotonaldehyde. The acetic acid content was found by titration with alkali in the presence of phenolphthalein.

SUMMARY

1. It was shown that the effect of anions of salts on the vapor-phase hydration of acetylene was only observed when the composition of the catalyst included a cation capable of activating acetylene or a hydrogen ion (proton). In the presence of an inactive cation (for example $Ca^{\cdot\cdot}$) the anions showed practically no effect.

2. The nature of the anion in cadmium salts apparently has no effect on the primary acts of acetylene activation and the formation of a polar complex. The action of the anion on the character of acetylene hydration is expressed qualitatively by a greater or lesser capacity to cause the conversion of acetaldehyde into side products.

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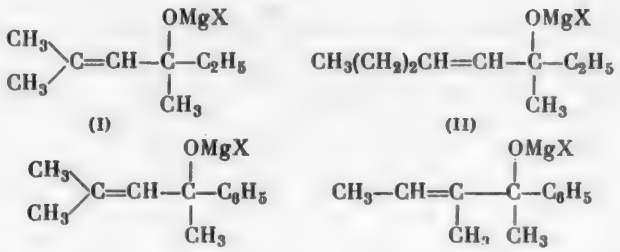
** Zbl. = Zentralblatt; C.A. = Chem. Abs.

VIII. SYNTHESIS OF PHENYLATED α,β-UNSATURATED ALCOHOLS AND DIENE (1, 3) HYDROCARBONS

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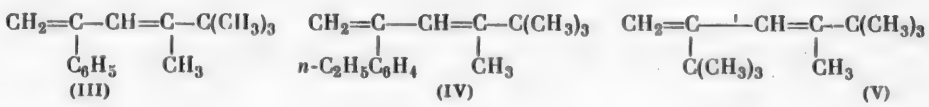
A study of the interaction of α,β-unsaturated ketones with RMgX showed that the halomagnesium carbinolates formed very frequently lost HOMgX and therefore diene (1, 3) hydrocarbons or mixtures of carbinols with hydrocarbons were obtained instead of tertiary carbinols [1]. This phenomenon was observed in the action of both AlkMgX and ArMgX and apparently did not depend on the nature of RMgX* or on the nature of the alkyl and aryl radicals attached to the carbinol carbon, as can be seen from a comparison of certain halomagnesium carbinolates, of which (I) loses HOMgX more readily than (II):



(I) (II)

Since $(R)_3COMgX$, obtained from mesityl oxide, lost HOMgX [2] more readily than $(R)_3COMgX$, obtained from α,β-unsaturated ketones able to exist in the form of cis- and trans-isomers [1, 3], then the stability of the $(R)_3COMgX$ examined should be considered as depending on the nature of the form (cis- or trans-) in which the α,β-unsaturated ketones react. This problem could be solved by a special investigation with pure cis- and trans-forms of α,β-unsaturated ketones.

In the present work we describe the interaction of RMgX with 2,2,3-trimethyl-5-arylpenten-3-ones-5 (Ar = C_6H_5, p-$CH_3C_6H_4$, p-$C_2H_5C_6H_4$), capable of existing in cis- and trans-forms [4]. The experiments showed that of the three homologous ketones, 2,2,3-trimethyl-5-p-tolylpenten-3-one-5 gave the greatest yields of tertiary alcohols, which were found to be difficult to dehydrate. In the Grignard reaction, the first and the last ketone gave mainly diene (1, 3) hydrocarbons. These features apparently are also explained by the effect of the steric factor. In comparison with the aliphatic analog (V) [3], the phenylated diene (1, 3) hydrocarbons of structure (III) and (IV) obtained



(III) (IV) (V)

show greater autonomy of the double bond in the 3,4-position and therefore are brominated (see table) with the elimination of a large amount of HBr.

*The effect of the amount of RMgX introduced into the reaction was studied.

Expt. No.	Sample (in g)	Amount of Br – CCl_4 solu. (in ml)	Amount of 0.1 N $Na_2S_2O_3$ solution (in ml)			Iodine number (theoretical)	Values of iodine numbers found			Conversion of bromine into HBr in % of total bromine consumption
			consumed in titra. of excess halide	corresponding to halide consump.	consumed on iodine from HI		total	elimination	addition	
			2,2,3-Trimethyl-5-p-tolylhexen-3-ol-5							
1	0.0462	4	11.17	4.48	0.32	109.25	123.08	17.58	105.80	7.14
			2,2,3-Trimethyl-5-p-tolylhepten-3-ol-5							
2	0.0517	4	10.34	5.31	0.57	103.04	130.36	27.98	102.38	10.73
			2-Phenyl-4,5,5-trimethylhexadiene-1,3							
3	0.1004	2.5	0.03	9.78	2.44	253.46	123.76	61.69	62.07	24.92
4	0.1006	6.0	4.28	19.20	5.22	—	242.24	131.72	110.52	27.18
			2-p-Ethylphenyl-4,5,5-trimethylhexadiene-1,3							
5	0.0810	1.75	0.57	6.28	1.67	222.33	98.28	52.34	[illegible]	26.59
6	0.0978	4.2	0.50	15.92	4.38	—	206.62	113.79	92.83	27.51

EXPERIMENTAL

1. Synthesis of 2,2,3-Trimethyl-5-p-tolylhexen-3-ol-5 and 2,2,3-Trimethyl-5-p-tolylheptene-3-ol-5.* a) Over a period of 4 hours, a solution of 8.5 g of 2,2,3-trimethyl-5-p-tolylpenten-3-one-5 in 20 ml of absolute ether and a solution of methylmagnesium iodide, prepared from 1.2 g of magnesium, 8 g of methyl iodide and 45 ml of absolute ether, were added to 100 ml of absolute ether at -15°. The reaction mass was carefully decomposed with 50 ml of ice water and a solution of dilute (1 : 3) acetic acid. The ether solution of the reaction products was washed with soda solution and water. After filtration the ether was removed by distillation and the residue recrystallized from boiling ethanol. We obtained 4 g (43.9%) of a substance in the form of needles with m.p. 136°.

Found %: C 82.56; H 10.58; OH 6.98. $C_{16}H_{24}O$. Calculated %: C 82.70; H 10.41; OH 7.32.**

b) Over a period of 4 hours, a solution of 10 g of 2,2,3-trimethyl-5-p-tolylpenten-3-one-5 in 20 ml of absolute ether and a solution of ethylmagnesium bromide, prepared from 1.8 g of magnesium, 9 g of ethyl bromide and 60 ml of absolute ether, were added to 100 ml of absolute ether at -15°. After the usual processing the reaction mixture yielded 3.8 g (33.3%) of a substance in the form of needles with m.p. 137°.

Found %: C 82.70; H 10.84; OH 6.70. $C_{17}H_{26}O$. Calculated %: C 82.87; H 10.63; OH 6.90.**

Dehydration of the carbinols by distillation at 4 mm with traces of iodine was accompanied by strong decomposition and therefore we were unable to isolate the diene (1, 3) hydrocarbons corresponding to them in sufficient amounts for investigation.

2. Synthesis of 2-Phenyl-4,5,5-trimethylhexadiene-1,3.*** Over a period of 4 hours, a solution of 20 g of 2,2,3-trimethyl-5-phenylpenten-3-one-5 in 20 ml of absolute ether and a solution of methylmagnesium iodide, prepared from 4.8 g of magnesium, 32 g of methyl iodide and 100 ml of absolute ether were added to 100 ml of absolute ether at -15°. The reaction mixture was left to stand for 12 hours. The reaction products were processed as above. After removal of the ether, the residue was dehydrated by distillation with a small amount of iodine at 5 mm. The hydrocarbon was purified by distillation over metallic sodium at 5 mm. We obtained 4.5 g (22.7%) of hydrocarbon.

*With the help of the student L. B. Sirotkin.

**For determination of iodine numbers see table.

***With the help of the student L. I. Stashkov.

B.p. 114° (5 mm), d_4^{20} 0.8980, $n^{20}D$ 1.5230, MR_D 68.14; calc. 66.93.

Found %: C 89.60; H 10.31. $C_{15}H_{20}$. Calculated %: C 89.94; H 10.06.

To 1 g of hydrocarbon was added 0.5 g of freshly distilled maleic anhydride; no reaction was observed in the cold but heating to 65° gave a solution with a characteristic yellow-green color and an exothermal reaction began with the temperature rising to 163°. The crystalline adduct was not examined more closely. The iodine numbers of the hydrocarbons were determined by MacIlliney's method with 50 and 100% bromine standards (see table, experiments 3 and 4).

3. Synthesis of 2-p-Ethylphenyl-4,5,5-trimethylhexadiene-1,3.* The synthesis was carried out similarly to synthesis 2, starting from 28 g of 2,2,3-trimethyl-5-p-ethylphenylpenten-3-one-5 and methylmagnesium iodide, prepared from 4.8 g of magnesium. We obtained 6 g (21.6%) of hydrocarbon.

B.p. 118° (2 mm), d_4^{20} 0.8964, $n^{20}D$ 1.5205, MR_D 77.50; calc. 76.17.

When a mixture of 1 g of hydrocarbon and 0.5 g of freshly distilled maleic anhydride was heated, an exothermal reaction was observed with a temperature rise to 150°. We obtained a crystalline adduct (needles) with m.p. 129-130° (decomp.).

Found: M 320.73. $C_{21}H_{26}O_3$. Calculated: M 326.42.

The hydrocarbon was brominated with 50 and 100% bromine standards (see table, experiments 5 and 6).

SUMMARY

1. We prepared the new α,β-unsaturated tertiary alcohols 2,2,3-trimethyl-5-p-tolylhexen-3-ol-5 and 2,2,3-trimethyl-5-p-tolylhepten-3-ol-5 and determined their physicochemical constants.

2. We prepared the new phenylated 1,3-diene hydrocarbons 2-phenyl-4,5,5-trimethylhexadiene-1,3 and 2-p-ethylphenyl-4,5,5-trimethylhexadiene-1,3, determined their physicochemical constants and studied their behavior in bromination.

3. A hypothesis was put forward that the stability of the halomagnesium carbinolates formed during the Grignard reaction depends on the cis-trans isomerism of the α,β-unsaturated ketones.

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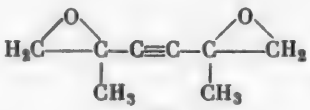
I. INVESTIGATIONS IN THE FIELD OF DIOXIDES OF THE ACETYLENE SERIES

F. Ya. Perveev and V. Ya. Statsevich

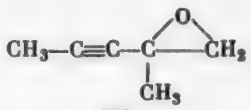
Leningrad State University

A new reaction of acetylene α-oxides with amines, leading to the formation of pyrrole homologs, was recently discovered [1]. The present work was directed at investigating the interaction of acetylene dioxides with amines. It seemed interesting to compare the reactivities of dioxides and monoxides of the acetylene series, to establish the order of opening of the oxide ring under the action of amines and to study the conditions for converting the diaminoglycols formed into the corresponding β-aminopyrrylcarbinols. This investigation was also necessary since homologs of pyrrole with this structure have not been described in the literature up to now and methods for their preparation are unknown. Further, since dioxides of the acetylene series have been studied very little, we decided to investigate the order of opening of the oxide rings under the action of alcohols with alkaline and acid catalysis.

As the subject for investigation, we chose the dioxide 2,5-dimethyldioxido -1,2;5,6-hexyne-3 (I).*



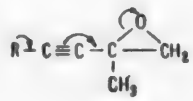
(I)



(II)

By studying the interaction of dioxide (I) with ammonia, methylamine and ethylamine, it was established that it was more reactive than monoxides of the acetylene series. For example, monoxide (II) reacted with ammonia and amines only when heated in sealed tubes at 100°, while dioxide (I) reacted with ammonia readily even at room temperature and with methylamine (without cooling) with an explosion.

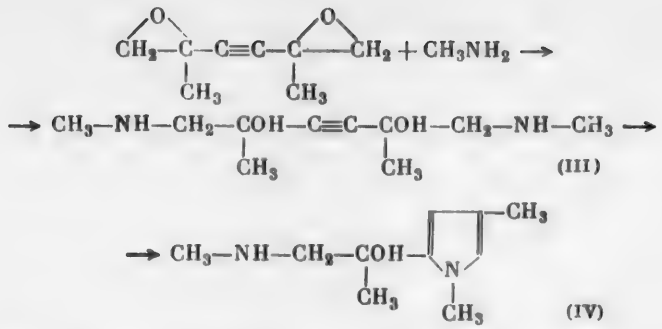
The increased reactivity of dioxide (I) is apparently explained by the fact that the electron density in the sphere of the oxide rings is decreased in comparison with monoxides of the acetylene series due to the absence of electron-donor substituents R:



The decrease in electron density in the sphere of the oxide ring facilitates the approach of a nucleophilic reagent to the reaction center.

The reaction of methylamine with dioxide (I) at room temperature formed 1,6-dimethylamino-2,5-dimethylhexyne-3-diol-2,5 (III), which gave N-methyl-2-(1-hydroxy-2-methylaminoisopropyl)-4-methylpyrrole (IV) when heated for many hours.

*B.p. 95-96° at 12 mm and $n^{20}D$ 1.4665 [2].



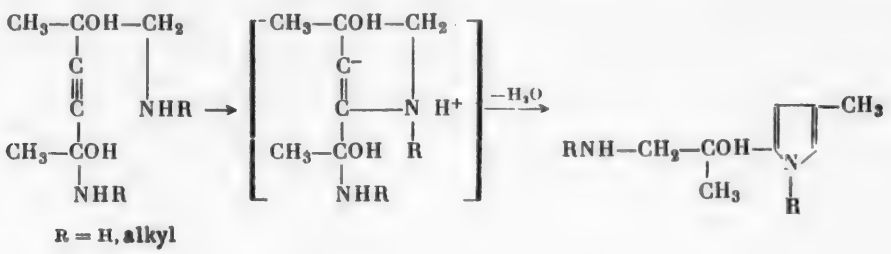
On analysis of the infrared spectra of compound (III) in the region of 1700-600 cm^{-1}, an absorption band was found at 1150 cm^{-1}, the characteristic frequency of a tertiary alcohol group [3] and also absorption bands characteristic of other groups of this compound. Compound (IV) gave a color reaction, mercury derivative and azo dye, characteristic of pyrroles. Analysis of the infrared absorption spectra showed absorption bands of a pyrrole ring (769, 1146, 1416 cm^{-1} [4, 5], a tertiary hydroxyl (1150 cm^{-1}) and of other groups.

Thus, the absence of absorption bands characteristic of a primary hydroxyl from the spectra of compounds (III) and (IV) and also the capacity of compound (III) to be converted into pyrrole indicates that opening of the oxide rings in compound (II) under the action of amines proceeds at the more hydrogenated carbon atom.

The synthesis of (IV) may be accomplished in one stage without preliminary isolation of the diaminoglycol by heating the starting components for many hours in a sealed tube. In a similar way we isolated N-ethyl-2-(1-hydroxy-2-ethylaminoisopropyl)-4-methylpyrrole (V), the reaction product of dioxide (I) with ethylamine.

Compounds (IV) and (V) were stable; they were oxidized only on prolonged storage. 2-(1-Hydroxy-2-aminoisopropyl)-4-methylpyrrole, formed by the action of ammonia on dioxide (I), was a very unstable compound, which rapidly polymerized. This difference is explained firstly by the fact that in the case of N-substituted β-aminopyrrylcarbinols there is no hydrogen whose lability facilitates various conversions and secondly by the fact that an electron-donor substituent in the N-position stabilizes the pyrrole ring due to an increased conjugation effect in the ring.

As regards the mechanism of β-aminopyrrylcarbinol formation from diaminoglycols, it may be regarded as an intramolecular nucleophilic substitution process:

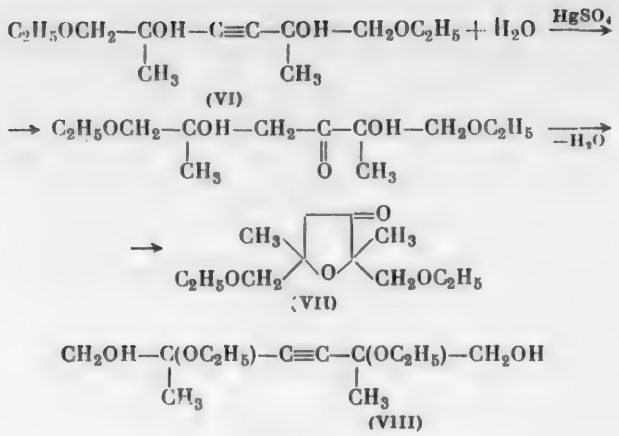


R = H, alkyl

Depending on the nature of the catalyst, the condensation of alcohol with dioxide (I) formed products differing both in physical constants and in chemical properties. In the case of alkaline catalysis, 1,6-diethoxy-2,5-dimethylhexyne-3-diol-2,5 (VI) was obtained.

Compound (VI) did not form phenylurethans with phenyl isocyanate. For proof of the structure, compound (VI) was converted into 2,5-dimethyl-2,5-diethoxymethylketo-3-hydrofuran (VII) by the Dupont reaction [6].

Acid catalysis yielded 2,5-diethoxy-2,5-dimethylhexyne-3-diol-1,6 (VIII), which reacted readily with phenyl isocyanate, giving the corresponding diphenylurethan. Compound (VIII) was not converted into a keto-hydrofuran by Dupont's method.



(VI)

(VII)

(VIII)

EXPERIMENTAL

1,6-Dimethylamino-2,5-dimethylhexyne-3-diol-2,5 (III). 15 g of dioxide (I), 8 g of methylamine and a few drops of water in a sealed tube were placed in a water bath (15-16°). The reaction mixture in the tube crystallized completely. After 24 hours, the crystalline mass formed was recrystallized from toluene. The substance obtained formed fine white crystals, which dissolved in water and alcohol, but were insoluble in ether. The m.p. was 109°.

Found %: C 59.95; H 10.08; N 14.29. $C_{10}H_{20}O_2N_2$. Calculated %: C 59.97; H 10.06; N 13.99.

Treatment of the substance with picric acid in alcohol gave a picrate in the form of yellow crystals with decomp. p. 193° (recrystallized from alcohol).

N-Methyl-2-(1-hydroxy-2-methylaminoisopropyl)-4-methylpyrrole (IV). 15 g of dioxide (I), 8 g of methylamine and a few drops of water in a sealed tube were placed in a water bath (15-16°) for several hours. The reaction mixture was then heated on a boiling water bath for 20 hours. Two vacuum distillations yielded 5 g of substance. The product was a viscous, yellow liquid, which was insoluble in water but dissolved readily in organic solvents.

B.p. 95-98° (1 mm), d_4^{20} 1.0285, $n^{20}D$ 1.5186, MR_D 53.76; calc. 54.31.

Found %: C 66.05; H 9.94; N 15.69, 15.30; act. H 1.02, 1.13. $C_{10}H_{18}ON_2$. Calculated %: C 65.93; H 9.89; N 15.36; one active H.

When treated with an aqueous solution of SeO_2, the substance gave the violet color characteristic of pyrroles. The mercury derivative melted with decomposition at 93°. Reaction with sulfophenyldiazonium chloride in alcohol yielded an azo dye as a red powder, melting with decomposition at 250°.

N-Ethyl-2-(1-hydroxy-2-ethylaminoisopropyl)-4-methylpyrrole (V). 6 g of dioxide (I), 3 g of ethylamine and a few drops of water in a sealed tube were heated on a boiling water bath (after preliminary cooling) for 15 hours. The product was vacuum distilled. We isolated 2.5 g of a viscous, yellow liquid, which was insoluble in water but readily soluble in organic solvents. It gave characteristic pyrrole reactions.

B.p. 133-135° (0.5 mm), d_4^{20} 0.9840, $n^{20}D$ 1.5082, MR_D 63.73; calc. 63.55.

Found %: N 13.50, 13.41; act. H 1.18. $C_{12}H_{22}ON_2$. Calculated %: N 13.33; one active H.

1,6-Diethoxy-2,5-dimethylhexyne-3-diol-2,5 (VI). Into a round-bottomed flask with a mechanical stirrer and a reflux condenser were placed 12 g of dioxide (I), 30 ml of anhydrous alcohol and 0.5 g of NaOH. The reaction mixture was stirred and heated (60-70°) for 20 hours. Browning of the solution was observed. The alcohol was removed and the product vacuum distilled. We isolated 6 g of a yellow liquid of average viscosity, which was soluble in water and organic solvents.

B.p. 120-123° (1.5 mm), d_4^{20} 1.0121, $n^{20}D$ 1.4620, MR_D 62.55; calc. 61.94.

Found %: C 62.79, 62.54; H 9.35, 9.41; act. H 1.98, 2.03. $C_{12}H_{22}O_4$. Calculated %: C 62.595; H 9.625; two active H.

2,5-Dimethyl-2,5-diethoxymethylketo-3-hydrofuran (VII). 12 g of (VI), 60 g of water and 2.4 g of $HgSO_4$ were placed in a round-bottomed flask with a reflux condenser and heated on a boiling water bath for 1 hour. The product was extracted with ether. The ether solution was dried with $MgSO_4$. The ether was removed and the product vacuum distilled. We isolated 3.5 g of substance as a pale yellow, mobile liquid, which was insoluble in water, but readily soluble in organic solvents.

B.p. 71.5-73° (0.5 mm), d_4^{20} 0.9945, $n^{20}D$ 1.4393, MR_D 60.95; calc. 60.45.

Found %: C 62.55; H 9.59; act. H absent. $C_{12}H_{22}O_4$. Calculated %: C 62.595; H 9.625.

2,5-Diethoxy-2,5-dimethylhexyne-3-diol-1,6 (VIII). Into a round-bottomed flask with a mechanical stirrer were placed 30 ml of anhydrous alcohol and 2 drops of conc. H_2SO_4. 10 g of dioxide (I) was gradually added so that the temperature of the reaction mixture did not rise above 45°. The solution acquired a dark brown color. After 15 minutes, 1 g of sodium carbonate was added to the solution and the mixture stirred until the solution lightened (30 minutes). After removal of the excess alcohol, the product was vacuum distilled. We obtained 6 g of substance as a very viscous, yellow liquid, which was soluble in water and organic solvents.

B.p. 126-128° (1 mm), d_4^{20} 1.0406, $n^{20}D$ 1.4694, MR_D 61.68; calc. 61.94.

Found %: C 62.37, 62.54; H 9.381, 9.384; act. H 2.04, 2.08. $C_{12}H_{22}O_4$. Calculated %: C 62.595; H 9.625; two active H.

The substance formed a crystalline urea derivative with α-naphthyl isocyanate. Recrystallization from alcohol yielded white crystals with m.p. 141°.

SUMMARY

1. A new method was developed for preparing β-aminopyrrylcarbinols by the interaction of a dioxide, 2,5-dimethyldioxido-1,2;5,6-hexyne-3, with ammonia, methylamine and ethylamine.

2. By this method we synthesized N-methyl-2-(1-hydroxy-2-methylaminoisopropyl)-4-methylpyrrole.

3. The reaction of the dioxide with alcohol was studied. It was found that with alkaline catalysis, a primary diether of erythrol, namely 1,6-diethoxy-2,5-dimethylhexyne-3-diol-2,5, was formed and with acid catalysis, a tertiary diether, 2,5-diethoxy-2,5-dimethylhexyne-3-diol-1,6.

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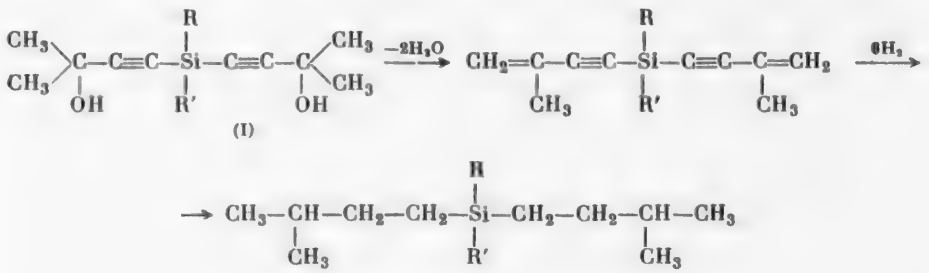
INVESTIGATIONS IN THE FIELD OF SYNTHESIS AND CONVERSIONS OF UNSATURATED ORGANOSILICON COMPOUNDS

II. SYNTHESIS OF SILICOHYDROCARBONS OF THE VINYLACETYLENE SERIES

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Institute of Organic Chemistry Academy of Sciences USSR and Institute of Petrochemical Processes Academy of Sciences Azerbaidzhan SSR

The synthesis of acetylene alcohols [1], their hydration and dehydration [2, 3] and also the addition of various reagents to them at the triple bond [1, 4, 5] is of great theoretical and practical interest. It seemed interesting to carry out the analogous conversions of organosilicon acetylene alcohols for a comparative study of their properties. We previously developed a method for preparing mono- [6], di- [7] and trihydric [8] γ-silicon-containing and γ-germanium-containing [9] acetylene alcohols. In the present investigation we studied the dehydration conditions of some γ-silicon-containing ditertiary acetylene glycols and also the catalytic hydrogenation of the silicohydrocarbons obtained by the scheme



(I)

EXPERIMENTAL

1. Dehydration of Bis-(1,1-dimethylpropyn-2-ol-1)-ethylsilane (III). We used 15 g (0.07 mole) of glycol, 0.03 g of hydroquinone and 13.7 g (0.1 mole) of $KHSO_4$. The reaction mixture was heated to 65° with continuous stirring. The reaction product was vacuum distilled three times. In this way we obtained four more silicohydrocarbons, whose characteristics are given in the table.

2. Quantitative Catalytic Hydrogenation of Bis-(2-methylbuten-1-yne-3)-diethylsilane (IV). 8.5 g of silicohydrocarbon, 30 ml of anhydrous methanol and 0.8 g of Raney nickel were placed in a hydrogenation "duck". The air was flushed from the system and after 5 minutes, the absorption of hydrogen began. The hydrogenation proceeded rapidly. A total of 6050 ml of hydrogen was absorbed instead of the theoretically required 5940 ml. After 3 hours the absorption of hydrogen ceased. After removing the catalyst and evaporating the methanol, we isolated the product of exhaustive hydrogenation.

B.p. 93-94° at 3 mm, $n^{21}D$ 1.4525, d_4^{20} 0.8358; MR_D 73.75; calc. 73.20.

Compound No.	Formula of silicohydrocarbon	Name	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	MR_D found	MR_D calculated	Found (in %) C	Found (in %) H	Found (in %) Si	Empirical formula	Calculated (in %) C	Calculated (in %) H	Calculated (in %) Si	Yield (in %)
(II)	$[CH_2{=}\underset{\displaystyle CH_3}{\underset{\vert}{C}}{-}C{\equiv}C]_2Si(CH_3)_2$	Bis-(2-methylbuten-1-yne-3)-dimethylsilane	75—75.5° (4)	1.5000	0.8475	65.36	63.13	75.89, 76.02	8.70, 8.56	15.45, 15.56	$C_{12}H_{16}Si$	76.52	8.56	14.91	54.8
(III)	$[CH_2{=}\underset{\displaystyle CH_3}{\underset{\vert}{C}}{-}C{\equiv}C]_2SiHC_2H_5$	Bis-(2-methylbuten-1-yne-3)-ethylsilane	76—77 (4)	1.5010	0.8518	65.15	65.11	76.50, 67.63	8.68, 8.82	15.00	$C_{12}H_{16}Si$	76.52	8.56	14.91	83.3
(IV)	$[CH_2{=}\underset{\displaystyle CH_3}{\underset{\vert}{C}}{-}C{\equiv}C]_2Si(C_2H_5)_2$	Bis-(2-methylbuten-1-yne-3)-diethylsilane	105 (6)	1.5027	0.8594	72.68	72.47	77.30, 77.47	9.32, 9.28	13.37, 13.00	$C_{14}H_{20}Si$	77.70	9.31	12.98	70.3
(V)	$[CH_2{=}\underset{\displaystyle CH_3}{\underset{\vert}{C}}{-}C{\equiv}C]_2\overset{\displaystyle CH_3}{\overset{\vert}{Si}}{-}C_2H_5$	Bis-(2-methylbuten-1-yne-3)-methylethylsilane	87—88 (2)	1.5000	0.8583	69.79	76.85 76.90	8.85, 14.10	14.20	77.15	$C_{13}H_{18}Si$	8.96	13.96	13.88	65.00
(VI)	$[CH_2{=}\underset{\displaystyle CH_3}{\underset{\vert}{C}}{-}C{\equiv}C]_2\overset{\displaystyle CH_3}{\overset{\vert}{Si}}{-}C_3H_7$	Bis-(2-methylbuten-1-yne-3)-methylpropylsilane	113 (10)	1.4990	0.8555	74.25	72.42	77.16, 77.35	9.21, 9.19	13.16, 13.24	$C_{14}H_{20}Si$	77.70	9.31	12.98	70.6

The fully hydrogenated diethyldiisoamylsilane obtained did not decolorize bromine water.

SUMMARY

1. A method was developed for preparing vinylacetylene silicohydrocarbons by dehydration of appropriate ditertiary γ-silicon-containing acetylene glycols in the presence of $KHSO_4$.

2. Bis-(2-methylbuten-1-yne-3)-ethylsilane, bis-(2-methylbuten-1-yne-3)-diethylsilane, bis-(2-methylbuten-1-yne-3)-dimethylsilane, bis-(2-methylbuten-1-yne-3)-methylethylsilane and bis-(2-methylbuten-1-yne-3)-methylpropylsilane were prepared and characterized for the first time.

3. Catalytic hydrogenation of bis-(2-methylbuten-1-yne-3)-diethylsilane yielded the corresponding saturated silicohydrocarbon, diethyldiisoamylsilane.

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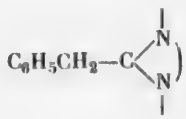
*Original Russian pagination. See C. B. Translation.

SYNTHESIS OF 3- AND 3,5-SUBSTITUTED THIAZOLES-1,2,4

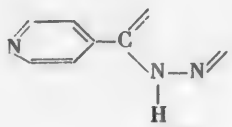
I. Ya. Postovskii and N. N. Vereshchagina

Ural Polytechnic Institute

2-Benzylbenzimidazole [1] and 2-benzylimidazoline [2] are highly active agents for lowering blood pressure. These compounds contain the characteristic grouping (I). In this connection it seemed interesting to synthesize analogous heterocyclic compounds with the same grouping such as, for example, 1,2,4-triazoles with benzyl residues in positions 3 and 3,5 (VI)* for pharmacological testing. It also seemed interesting to synthesize 1,2,4-triazoles with a γ-pyridyl residue for testing the tuberculostatic properties, since such a compound would contain the grouping (II), which is present in the active hydrazide of isonicotinic acid or the corresponding hydrazones.

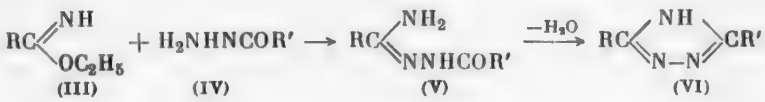


(I)



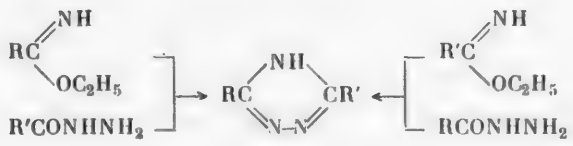
(II)

Several methods are described in the literature for preparing 3,5-substituted triazoles-1,2,4. Thus, they may be obtained by fusing acid amides and hydrazides [3], by heating N^1, N^2-diacylhydrazines with zinc ammonium chloride [4] and by the reaction of nitriles with the salt of hydrazides of benzenesulfonic acid [5] (see also [6]). Since most of the existing methods of preparing the triazoles described above give poor yields, we considered it worthwhile to develop a new method synthesizing these compounds making it possible to prepare with certainty various 3- and 3,5-derivatives of triazoles-1,2,4. It was found that a suitable method for this purpose was that by which triazoles were obtained by the reaction of iminoethers (III) with acid hydrazides (IV) through the stage of acylamidrazones (V) by the scheme



(III) (IV) (V) (VI)

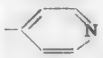
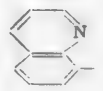
If R = H (in the case of the hydrazide of formic acid) then monosubstituted triazoles were formed. By this method, each disubstituted triazole could be obtained by two routes as is shown by the scheme



*In formula (VI) the hydrogen atom is arbitrarily placed at nitrogen atom 4. In actual fact, the position of the hydrogen atom in different triazole derivatives has not been determined.

TABLE 1

Acylamidrazones $R-C(=NNHCOR')-NH_2$

Compound No.	R	R'	Yield, calculated on hydrazide (in %)	Melting point	Empirical formula	Nitrogen content (in %) found	Nitrogen content (in %) calculated
1	CH_3	CH_3	50	175—176°	$C_4H_9ON_3$	36.63	36.50
2	CH_3	C_6H_5	66	168—169*	$C_9H_{11}ON_3$	23.27	23.72
3	CH_3	$C_6H_5CH_2$	46	166—167	$C_{10}H_{13}ON_3$	21.81	21.98
4	CH_3		74	163—164*	$C_8H_{10}ON_4$	31.22	31.45
5	C_6H_5	CH_3	58	172—173	$C_9H_{11}ON_3$	23.56	23.72
6	C_6H_5	C_6H_5	50	183—184 (188[8])	$C_{14}H_{13}ON_3$	—	—
7	C_6H_5	$C_6H_5CH_2$	28	176—177	$C_{15}H_{15}ON_3$	16.63	16.59
8	C_6H_5		80	175—176	$C_{13}H_{11}ON_4$	23.52	23.32
9	$C_6H_5CH_2$	CH_3	81	181—182	$C_{10}H_{13}ON_3$	21.75	21.98
10	$C_6H_5CH_2$	C_6H_5	50	179—180	$C_{15}H_{15}ON_3$	16.61	16.59
11	$C_6H_5CH_2$	$C_6H_5CH_2$	34	182—183	$C_{16}H_{17}ON_3$	15.71	15.72
12	$C_6H_5CH_2$		50	182—183	$C_{14}H_{14}ON_4$	22.08	22.04
13	$C_6H_5CH_2$		37	166—168*	$C_{18}H_{16}ON_4$	18.16	18.41

* This compound crystallized with a molecule of water, which was removed by drying at 110°.

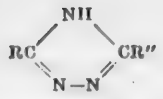
Thus, of the two different iminoethers and the two hydrazides, it is possible to choose the most accessible ones for synthesis.

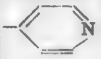
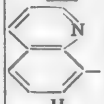
As starting materials for the synthesis of triazoles, in the present work we used methyl iminoether, benzoiminoether, benzyl iminoether and the hydrazides of formic, acetic, benzoic, phenylacetic, isonicotinic and 8-quinolinecarboxylic acids. The reaction was carried out in boiling alcohol solution. The first stage of the reaction formed the acylamidrazones (V) (Table 1), which lost a molecule of water when heated above their melting points and gave good yields of triazoles (VI) (Table 2). The rate of formation of the triazoles from the acylamidrazones varied and depended on the nature of the radicals. In the case of the hydrazide of formic acid, ring closure proceeded so readily that it was even impossible to isolate the intermediate product, formylamidrazone. Even on boiling in alcohol, ring closure occurred with the acylamidrazone containing an isonicotinyl residue (Table 1, compounds 4, 8 and 12). All the other acylamidrazones underwent ring closure with more difficulty, i.e., only on heating above their melting points. Some of the triazoles presented here have been described in the literature (compounds 14, 15, 18, 19, 24 and 28), but they were obtained by other methods. We prepared three of the triazoles presented in Table 2 by the alternate routes described above (compounds 15 and 18, 16 and 22 and 20 and 23).

The acylamidrazones and triazoles were readily crystallizable, colorless compounds. The triazoles had amphoteric properties: they dissolved in alkalis due to the acid atom of the NH group and also in strong hydrochloric acid in the cold or on heating, apparently due to the basic properties of the other nitrogen atoms of the ring. The nature of the substituent affected the basicity of the triazoles. Thus, triazoles containing a methyl group in position 3 and another group in position 5 [compounds 14, 15 (18) and 16 (22)] and also triazoles with a pyridine residue (compounds 17, 21 and 25) and the monobenzyl derivative 27 gave readily crystallizable hydrochlorides, which were not hydrolyzed when aqueous solutions were heated. On the other hand, triazoles with phenyl residues (compounds 19 and 28) and with phenyl and benzyl residues [compound 20 (23)] and also dibenzyl and quinoline compounds (24 and 26) formed unstable, readily hydrolyzable hydrochlorides.

TABLE 2

3- and 3,5-Substituted Triazoles-1,2,4



Compound No.	R	R′	Yield (in %)	Recrystallization solvent	Melting point	Empirical formula	Nitrogen content (in %) found	Nitrogen content (in %) calculated	Melting point of picrate
14	CH_3	CH_3	90	Benzene	139—140° (142 [9])	$C_4H_7N_3$	43.06	43.27	168—169° (170 [11])
15	CH_3	C_6H_5	74	Toluene	163—164 (166 [3])	$C_9H_9N_3$	—	—	157—159 (158 [3])
16	CH_3	$C_6H_5CH_2$	95	Aqueous alcohol	136—137	$C_{10}H_{11}N_3$	24.19	24.26	148—150
17	CH_3		92	Water	207—208	$C_8H_8N_4$	34.78	34.98	223—224 (decomp.)
18	C_6H_5	CH_3	74	Toluene	162—163 (166 [3])	$C_9H_9N_3$	—	—	157—159 (158 [3])
19	C_6H_5	C_6H_5	92	Aqueous alcohol	189—190 (190 [3,5])	$C_{14}H_{11}N_3$	—	—	167—169 (166 [5])
20	C_6H_5	$C_6H_5CH_2$	84	Benzene, ligroin	113—114	$C_{15}H_{13}N_3$	17.73	17.86	197—198
21	C_6H_5		94	Aqueous alcohol	242—243	$C_{13}H_{10}N_4$	24.96	25.21	244—246 (decomp.)
22	$C_6H_5CH_2$	CH_3	75	The same	137—138	$C_{10}H_{11}N_3$	—	—	148—150
23	$C_6H_5CH_2$	C_6H_5	94	Benzene, ligroin	113—114	$C_{15}H_{13}N_3$	—	—	196—198
24	$C_6H_5CH_2$	$C_6H_5CH_2$	93		144—146 (147 [10])	$C_{16}H_{15}N_3$	16.93	16.86	134—135
25	$C_6H_5CH_2$		92	Aqueous alcohol	174—175	$C_{14}H_{12}N_4$	23.34	23.72	174—175
26	$C_6H_5CH_2$		90	The same	122—123	$C_{15}H_{14}N_4$	19.54	19.57	153—154
27	$C_6H_5CH_2$	H	43	Toluene	95—96	$C_9H_9N_3$	26.33	26.40	—
28	C_6H_5	H	18	The same	117—118 (120 [12])	$C_8H_7N_3$	—	—	168—169

Some triazoles were converted into acetyl derivatives by reaction with acetic anhydride. Thus, we obtained readily crystallizable acetyl compounds from triazoles 23 (m.p. 100-101°) and 25 (m.p. 109-111°). All the triazoles gave bright yellow picrates (see Table 2 for melting points of picrates).

By testing the tuberculostatic properties of the acylamidrazones and triazoles with a γ-pyridine residue it was established that the acylamidrazones (4, 8 and 12) stopped the growth of tubercle bacilli at a dilution of 1:1,000,000, while the cyclic products obtained from them, the triazoles (7, 21 and 25), were inactive compounds.* This is evidently explained by the fact that the acylamidrazones contained the amide group CONH⁻, capable of enolization and complex formation with metals, while this group was absent from the triazoles. The results of the testing again indicate the value of this group in derivatives of γ-pyridylhydrazide for producing tuberculostatic properties [7].

*The tuberculostatic properties of the compounds were tested by É. I. Chertkova (Sverdlovsk Tuberculosis Scientific Research Institute). The results of pharmacological testing of the benzyl derivatives will be published separately.

EXPERIMENTAL

Preparation of Acylamidrazones. 0.001 mole of NaOH was dissolved in anhydrous alcohol by boiling. To the cooled solution was gradually added 0.001 mole of iminoether hydrochloride with shaking. The precipitated mineral salt was removed and to the filtrate was added 0.001 mole of hydrazide. The mixture was boiled for 5-10 minutes and left to cool for 30-40 minutes. When a precipitate did not form on cooling, the solution was diluted with water. The precipitate was collected, dried and recrystallized from 95% alcohol (compound 2 from a mixture of alcohol and benzene and compound 3 from aqueous alcohol). All the acylamidrazones melted with the evolution of bubbles (water vapor) and the formation of triazoles. The acylamidrazones obtained, the yields, melting points and analyses are presented in Table 1.

Preparation of 3- and 3,5-Substituted Triazoles 1,2,4. The acylamidrazone was heated in a small flask immersed in Wood's alloy at a temperature 5-10° above the melting point until the evolution of water vapor bubbles ceased. After cooling, the triazole was recrystallized from the solvent indicated in Table 2, which also gives the analyses and data on the yields and melting points of the triazoles and their picrates.

SUMMARY

1. A convenient method is put forward for preparing 3- and 3,5-substituted triazoles-1,2,4, starting from iminoethers and hydrazides of acids.

2. By this method we synthesized 13 acylamidrazones and 12 triazoles, of which 12 acylamidrazones and 7 triazoles have not been described in the literature.

3. The importance of a free amide group in γ-pyridyl derivatives of acylamidrazones for producing tuberculostatic activity was demonstrated.

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A CONTRIBUTION ON THE PROPERTIES AND STRUCTURE OF PLASTEINS

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Since the discovery by Danilevskii [1], there has been repeated confirmation of the capacity of pepsin, trypsin, cathepsin, chymotrypsin, papain and enzyme extracts of various organs and tissues to act on incomplete hydrolyzates of protein (peptones) to synthesize peculiar proteinaceous substances, which have been named plasteins [2]. Up to the present time, plasteins have been synthesized from hydrolyzates of fibrin, keratin, casein and myosin [3, 4], egg albumin [2, 5], globulins [6, 7], zein and gliadins [8, 9], trypsin and pepsin [10], insulin [11] and other proteins. It was established that plastein formation may occur in hydrolyzates with various degrees of cleavage, at various temperatures (within the limits of heat stability of the enzymes) and over comparatively wide pH limits, specific for each enzyme. Accompanied by the synthesis of peptide bonds [7] and an increase in the molecular weight [8, 12], the formation of plasteins under various conditions stopped at a more or less definite stage of coagulation of the particles of the hydrolyzate with a considerable excess of the latter. In physicochemical properties the plasteins from various hydrolyzates are a group which are in many ways similar to proteinaceous substances, lacking the specific properties of the mother proteins. This circumstance shows the known deficiency of the plastein formation reaction. On the other hand, its widespread applicability presupposes the existence of much greater possibilities for this enzyme reaction. As is known by the action of enzymes on hydrolyzates under high pressure, Bresler et al [13] synthesized quasi-proteins with properties similar to those of the starting proteins. Regrettably, such a factor in the synthesis is unnatural. The capacity of proteolytic enzymes to synthesize plasteins is undoubtedly closely related to the more extensive participation of enzymes in the synthesis of proteins in an organism. In this connection, a thorough study of the properties and structure of plasteins and the mechanism of their synthesis is apparently one of the essential steps in the study of proteins. Nonetheless, many of the properties of plasteins and, in particular, the problem of the structure of the hydrolyzate peptides and their rearrangement during the synthesis have been studied very little. Thus, on investigating the plastein from zein, in their first paper [14] Virtanen et al. agree with the opinion put forward earlier by Folly [15] that plastein formation was the process of cyclization of hydrolyzate peptides. However, in their subsequent paper [8], they refuted this opinion and described plastein as a substance consisting of open polypeptides with 36-100 amino acid residues. Gavrilov et al. [16], on observing the simultaneous decrease of amine nitrogen and the intensity of light absorption by copper complexes during plastein formation, considered that plastein synthesis is accompanied by cyclization to form diketopiperazines.

Having available data on the molecular weight of plasteins [12], we undertook an investigation to compare plasteins with the mother proteins by electrophoresis by Tiselius's method [17], with paper [18] and by electroreduction [19] in combination with spectrophotometry and determinations of the copper numbers [20]. The properties of the plasteins and the mother proteins were also characterized by determinations of the amine nitrogen, relative viscosity of solutions and titration numbers [21] and also by determining the toxic and anaphylactogenic properties in experiments on animals [22]. As mother proteins for the synthesis of plasteins, we chose two proteins which are widely distributed in the animal world and differ strongly in purpose and properties and these were water-insoluble, inhomogeneous casein and soluble, homogeneous human serum albumin. Some parts of the casein and the albumin were hydrolyzed with the juice of the mucosa of hog stomachs, others with pepsin and the third set with hydrochloric acid at pH 1.7 by Perov's method [21]. The plasteins were synthesized under the action of natural gastric juice of the dog and under the action of pure pepsin.

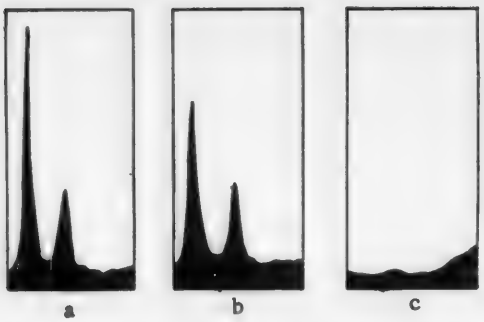


Fig. 1. Electrophoregrams (rise in boundaries). Electrophoresis at pH 8.6. a) Casein according to Hammarsten, b) casein according to Perov, c) plastein from casein.

Electrophoresis experiments showed the existence of great differences in the properties of the plasteins, the original hydrolyzates and the mother proteins. Especially great differences were found in the properties of plastein and casein. Plasteins synthesized from hydrolyzates of the inhomogeneous protein casein (Fig. 1,a and b; Fig. 2,a and b) were found to be electrophoretically homogeneous (Fig. 2,f, g and h) and have a higher electrophoretic mobility than the mother protein (Table 1). On electrophoresis, a mixture of casein and plastein separated into three fractions (Fig. 2,i), which corresponded to two casein fractions and one plastein fraction. The plasteins from casein were consequently new substances and not one of its fractions.

The plastein from serum albumin was also electrophoretically homogeneous (Fig. 3,d), but since the original protein was homogeneous (Fig. 3,a and b), the difference in their electrophoregrams showed only in the width of the peaks. The electrophoretic mobility of this plastein, like that of the plastein from casein, also exceeded that of the original protein (Table 1).

Electrophoresis on paper supplemented the characterization of the properties of plasteins. When the electrophoregrams were developed, the plasteins gave as good a color as the mother proteins. The hydrolyzates showed no color at all. At pH 8.6, the spots of plasteins did not move, apparently due to their lower solubility than the mother proteins. Experiments at pH 11.0 confirmed data from Tiselius electrophoresis on the number of fractions of albumin and casein and the homogeneity of the plastein from casein. The spot of the plastein from soluble protein albumin remained immobile at this pH also, clearly indicating the difference in the properties of the plasteins from different proteins.

Determination of the titration numbers also showed certain differences in the properties of the plasteins. The plastein obtained from the more acid protein casein reacted with a larger amount of alkali than the plastein from albumin. The acid function of the plasteins, consequently, depended directly on the properties of the

TABLE 1

Electrophoretic Properties of Plasteins

Substance investigated	pH of buffer solution	No. of fractions	Content (in %)		EP-mobility, in $cm^2/volt \cdot sec \cdot 10^{-5}$	
			1st fraction	2nd fraction	1st fraction	2nd fraction
Casein according to H.*	8.6	2	68.9	31.1	5.84	3.96
Casein according to P.**	8.6	2	64.1	35.9	5.95	4.16
Casein according to H.*	11.0	2	61.6	38.4	7.47	5.68
Casein according to P.**	11.0	2	67.8	32.2	7.33	5.55
Plasteins						
a) from enzyme hydrolyzate of casein*	11.0	Homogeneous	—	—	9.48	
b) the same, 2nd precip.	11.0	The same	—	—	9.70	
c) from acid hydrolyzate of casein*	11.0	» »	—	—	9.51	
d) from enzyme hydrolyzate of casein**	11.0	» »	—	—	9.53	
Albumin	8.6	» »	—	—	5.68	
The same	11.0	» »	—	—	8.87	
Plastein from albumin	11.0	» »	—	—	9.11	

*According to Hammarsten.

**According to Perov.

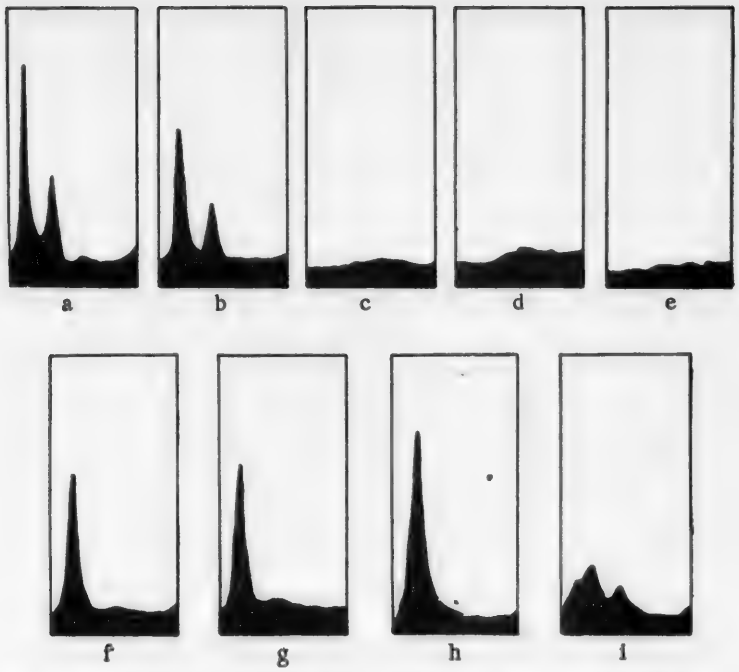


Fig. 2. Electrophoregrams (rise in boundaries). Electrophoresis at pH 11.0. a) Casein according to Hammarsten, b) casein according to Perov, c) casein hydrolyzate, d) hydrolyzate after plastein formation, e) casein after electroreduction. Plasteins: f) from enzyme hydrolyzate of casein, g) 2nd precipitation, h) from acid hydrolyzate of casein, i) mixture of plastein from casein with original protein.

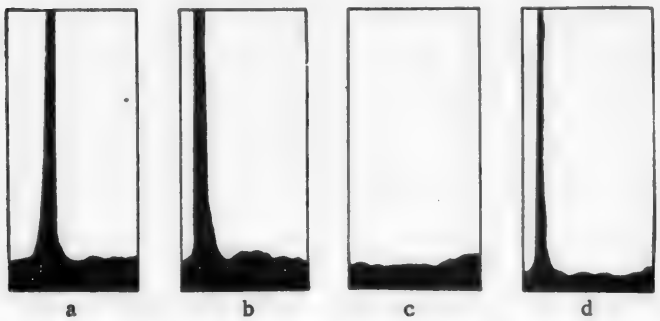


Fig. 3. Electrophoregrams (rise in boundaries). Electrophoresis at pH 11.0. a) Serum albumin (EP at pH 8.6), b) the same, c) albumin hydrolyzates, d) plastein from albumin.

mother proteins. (As shown above, with solubility there was an inverse dependence). The titration numbers of the plasteins were higher than the titration numbers of the mother proteins; this apparently explains their greater electrophoretic mobility.

The synthesis of plastein stopped when there was a considerable amount of externally unchanged hydrolyzate. After removal of the plastein formed, concentration of the hydrolyzate and the addition of fresh enzyme to it again formed plasteins, which were designated second precipitation plasteins. We also prepared such a plastein (from casein) and investigated it. According to the character of the electrophoregrams (Fig. 2,g) and the value of the electrophoretic mobility (Table 1), it was the same as the first precipitation plastein.

TABLE 2

Relative Extent of Plastein Synthesis

Amine nitrogen by Van Slyke method, 3 minute determination (in % of total)				Cleavage of protein (in %)	Amine acid residues in hydrol. peptide	Percent plastein synthesis
mother proteins	hydrolyzates		plasteins			
	enzyme	acid				
			Albumin			
0.73	14.05		6.43	13.38	7	57.60
			Casein			
2.94		9.30	3.02	7.31	16	98.74

TABLE 3

Amine Nitrogen Content in % of Total Nitrogen

Name of mother proteins	Original proteins	Hydrolyzates		Plasteins	
		enzyme	acid	from enzyme hydrolyzates	from acid hydrolyzates
	Duration of determinations (in min.)				
	3 15	3 15	3 15	3 15	3 15
Casein	2.94 6.19	11.14 14.03	9.30 21.82	2.94 6.18	3.02 5.84
Albumin	0.73 8.34	14.05 24.10	16.48	6.43 12.15	

Plasteins may be synthesized from hydrolyzates with various degrees of cleavage. Virtanen et al. [8] found that the size of the hydrolyzate particles affected the yield of plasteins. We observed greater relative synthesis of plasteins in hydrolyzates with larger peptides (Table 2). At the same time, plasteins from enzyme and acid hydrolyzates did not differ electrophoretically (Fig. 2,f and h) or in other properties. Apparently, the length of the hydrolyzate peptides only affected the plastein formation process from the quantitative point of view.

V. V. Zav'yalov [2] considered the existence of soluble forms of plastein possible. Electrophoresis of that part of the hydrolyzate which remained after the first plastein formation, after separation of the plastein precipitate, gave an electrophoregram (Fig. 2,d) which did not differ in any way from electrophoregrams of the normal hydrolyzate (Fig. 2,c). The existence of soluble plasteins was not confirmed by this experiment.

Investigation of plastein by electroreduction [19] showed that like the original protein it also contained nitrogen of cyclic forms of bonds, but in a smaller amount (16.28% in the plasteins with respect to the total nitrogen and 22.88% in the original protein). From these data and data on the content of α-amino nitrogen (results of formol titration of complete hydrolyzates) and ammonia nitrogen, we calculated [23] that for each cyclic two amino acid anhydride (diketopiperazine) in the plastein monomer there were 6.7 amino acids of peptide chains and for each cyclic anhydride of the original protein monomer there were only 4.3 amino acids of peptide chains. Consequently the structure of the plastein differed from that of the original protein. The peptide chains of the plastein were evidently longer.

Spectrophotometry of solutions of copper complexes of plasteins and original proteins of casein and serum albumin showed (Figs. 4 and 5) that in contrast to those of the original proteins, the absorption maxima of the plasteins were in the shorter wave part of the visible spectrum. By determining the copper numbers it was found that those of the plasteins had higher values than those of the mother proteins. According to an investigation of

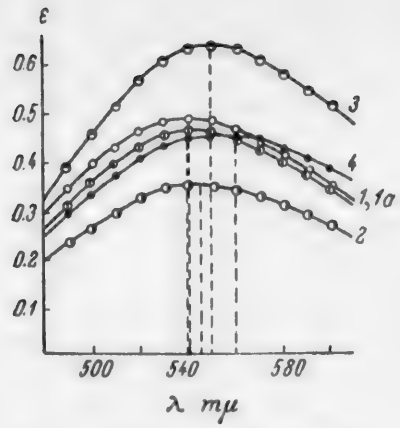


Fig. 4. Spectrophotometric curves of copper complexes. Plasteins: 1) from enzyme hydrolyzate of casein according to Hammarsten, 1a) from enzyme hydrolyzate of casein according to Perov, 2) from acid hydrolyzate of casein, 3) casein according to Hammarsten, 4) casein hydrolyzate.

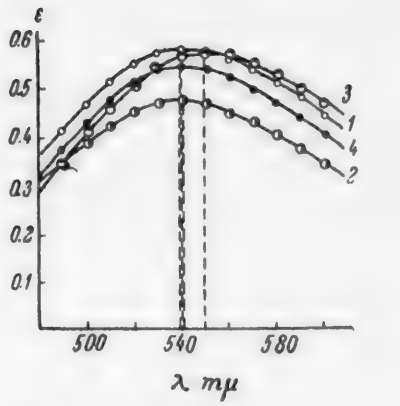


Fig. 5. Spectrophotometric curves of copper complexes. 1) Plastein from enzyme hydrolyzate of albumin, 2) plastein from acid hydrolyzate of albumin, 3) albumin, 4) albumin hydrolyzate.

a mixture of peptides [28], such a distribution of the light absorption maxima and the copper numbers of the plasteins and mother proteins indicated that the peptide chains of the plasteins were longer, which agreed with calculations from electroreduction data.

EXPERIMENTAL

1. Original Proteins. Casein was obtained by two methods, by Hammarsten's method and by Perov's method from separated milk. In the preparation according to the latter method, the protein concentrate after the first precipitation (10% CH_3COOH) was kept for 30 days in an alcohol – ether mixture and then subjected to 8 (or 12) reprecipitations at pH 4.7 with 10% HCl from alkali solution. Water was removed from the proteins with alcohol and alcohol with ether. The nitrogen content (by the Kjeldahl method) of different casein preparations obtained by the first method was 15.51-15.90% and by the second method, 15.46-15.67%. The blood serum (donor) albumin contained 15.86% of nitrogen.

2. Hydrolysis of Original Proteins. a) Enzyme. Casein was hydrolyzed by commercial gastric juice at pH 1.7 for 3 days; the protein concentration was 4%, the temperature 40° and the antiseptic, toluene. Albumin was hydrolyzed with high activity pepsin.

b) Acid hydrolysis. This was carried out by Perov's method with certain changes. 2% alkali solutions (pH 7-8) were adjusted to pH 1.7 with conc. HCl. The solutions were boiled under reflux for 10 hours and then the hydrolyzates were neutralized to the isoelectric pH of the protein. The unchanged protein residues were removed by filtration and the filtrates concentrated under vacuum at 50° to a concentration of 30-40%. Some of the hydrolyzates were dried in vacuum at 30°. Plasteins synthesized from concentrated and dried hydrolyzates were identical in properties.

3. Synthesis of Plasteins. The hydrolyzates were mixed with fresh, natural dog gastric juice in a volume ratio of 3:1 and 0.1 N HCl added to adjust the pH to 4.8-5.0 followed by toluene (antiseptic). The mixture was kept at 40° for 3 days. Most of the experiments on the synthesis of plasteins from albumin hydrolyzate were carried out with a solution of highly active pepsin. In all cases precipitates of plasteins began to form after 30-40 minutes. The plastein from casein hydrolyzate precipitated on the bottom of the vessel, but in the albumin hydrolyzate, it remained in a suspended state. Precipitates were not formed in control experiments without enzyme. At the end of the experiment, the plasteins were isolated by filtration and washed with water on the filter until the filtrate gave no reaction with CCl_3COOH. It was very difficult to isolate the plastein from the albumin hydrolyzate: the plastein clogged the filter. The water was removed from the plasteins with alcohol and the alcohol with ether. The nitrogen content (by the Kjeldahl method) of different batches of plasteins obtained a) from enzyme hydrolyzate of casein by Hammarsten's method was 14.16-15.03%, b) from the acid hydrolyzate of this protein, 14.16%, from the enzyme hydrolyzate of casein by Perov's method, 14.47-14.55% and from the enzyme hydrolyzate of albumin, 14.93-15.47%.

For the second precipitation of plastein, the hydrolyzate from the first precipitation was inactivated by 30 minutes heating on a water bath, filtered and concentrated to 30-40% and then fresh dog gastric juice was added. The nitrogen content of the second precipitation plasteins was 14.56%. The hydrolysis of the original proteins and the synthesis of plasteins were accompanied by the following changes in amine nitrogen (determined by the Van Slyke method in the apparatus of P. G. Ioanisiani [24], where a 3 minute determination equals a 5 minute one and a 15 minute determination equals a 30 minute one by the classical method). The results are given in Table 3. These show that the amino nitrogen of the plasteins from casein approximately equalled the amine nitrogen of the original proteins, while that of the plastein from albumin was considerably greater than that of the original protein.

Degree of Cleavage of Mother Proteins and Extent of Plastein Synthesis. The calculations were carried out from data on the amine nitrogen content (with respect to the total) according to the scheme presented in paper [13]. Taking the nitrogen of the mother protein as 100%, we calculated the amino nitrogen content present as the nitrogen (A) of its peptide chains. The difference between the amine nitrogen of the hydrolyzate and the protein gave the nitrogen (B) exposed in the hydrolysis of the peptide chains; the ratio B/A·100 gave the percentage cleavage. From the latter we found the average length of the hydrolysis peptides in amino acid residues. By subtraction of the amino nitrogen of the mother protein from the amino nitrogen of the plastein, we found the nitrogen (C) of the peptide bonds of the hydrolyzate remaining open during plastein synthesis. From the difference B − C we found the nitrogen (D) blocked during the synthesis of the peptide bonds. From the ratio D/B·100 we calculated the relative extent of plastein synthesis.

4. Titration Number (amount of 0.1 N NaOH in ml required for titrating 1 g of protein to phenolphthalein). With casein, the original protein showed an acid reaction. The number of COOH groups in this protein to NH_2 groups, according to data from the tables of Gorovits , is 129:102 = 1.26, a higher number than in other proteins. In this connection, the determination of the titration numbers was of particular interest. Samples of the substances investigated, weighing 0.1-0.3 g were dissolved in excess 0.1 N NaOH and the excess titrated with 0.1 N HCl. The titration numbers found (average) were as follows: plasteins from casein by Hammarsten's method − 11.70; mother protein − 9.30; plastein from casein by Perov's method − 11.67, mother protein − 9.19; plastein from albumin − 8.50, mother protein − 6.80.

5. Electrophoresis by Tiselius' Method was carried out at pH 11.0. This was determined by the fact that on dialysis against the most accepted veronal buffer solution with pH 8.6, the plasteins were almost completely precipitated. At the same time, we demonstrated that the high alkalinity of the buffer solution did not affect the electrophoretic properties of the substances investigated: both at pH 8.6 and at pH 11.0 casein and albumin gave analogous electrophoregrams (Figs. 1-3,a and b).

Solutions of Preparations and Their Dialysis. The concentration of the solutions was 2.5%. For electrophoresis at pH 8.6, samples of plastein, original protein and hydrolyzate (freeze-dried) were dissolved in buffer solution or 0.75% Na_2CO_3. For electrophoresis at pH 11.0, samples of these substances were mixed with 9 ml of buffer solution, 4% NaOH added to the mixture until the solid dissolved (about 0.5 ml) and the solution diluted to 10 ml with H_2O. The solutions were dialyzed in cellophane bags against buffer solutions at 2-3° for three days with the buffer solution changed twice a day. At the end of the dialysis and before electrophoresis, the solutions were centrifuged at 12,000 rev/min. Considering the low molecular weight of the plastein, its permeation through the cellophane was checked during the dialysis. The total nitrogen of the dialyzed plastein was 94.26% of the nitrogen of the undialyzed material. The original protein gave a corresponding value of 98.93%. Allowing for the difficulty of washing the plastein from the cellophane film, none of it was lost during dialysis.

EP Conditions and Results. The electrophoresis was carried out in an analytical cell of a Tiselius apparatus at 2-3° with a current strength of 8 ma , voltages of 70 and 80 volts and an experiment duration of 3-4 hours. We photographed the original position of the boundaries (rise and fall) and the position after two hours and at the end of the experiment. Electrophoregrams from electrophoresis at pH 8.6 and 11.0 are presented in Figs. 1-3. The electrophoretic mobility was calculated by the method presented in paper [25]. From determinations of the resistance of the dialyzed solution (on a Phillips bridge with "magic eye") we calculated the specific conductivity from the current strength and the cross-sectional area of the cell (q = 0.32 cm^2), the field strength was calculated and from the rate of movement of the peaks and the photographic coefficient, (q = 1) the electrophoretic mobility

was obtained in $cm^2/volt \cdot sec \cdot 10^{-5}$. The results are presented in Table 1. The percent content of the fractions was found by measuring the area of the peaks with a planimeter and the results are given in the same table.

6. Electrophoresis on Paper. Buffer solutions: 1) 55.23 g of veronal was dissolved in 650 ml of 0.4 N NaOH, the solution diluted to 3 liters with water and adjusted to pH 8.6 with acid or alkali as required; 2) the same amount of veronal, 0.4 N NaOH and water was adjusted to pH 11.0 with alkali. Chromatographic paper was used in the form of 30 × 3 cm strips with the working area 20 cm long. Portions (0.02 ml) of 3% solutions of the substances investigated were put onto the paper strips. An experiment lasted for 18 hours in a closed chamber at room temperature. The potential was 5 /cm and the current strength 0.2 ma/cm of the cross-section of the paper. The developer was bromophenol blue in mercuric chloride – acetic acid solution. An interesting rule was observed for casein at pH 8.6 in all experiments: the front fraction separated into three longitudinal bands which were always of constant size.

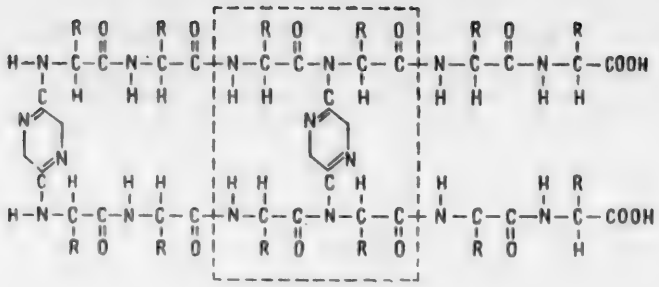
7. Spectrophotometry of Copper-Complex Solutions. A precipitate of $Cu(OH)_2$ was prepared by the action of 5% NaOH on 10% $CuSO_4$ solution; it was washed carefully with water. To 0.25 g of the substance investigated (plastein, original protein or freeze-dried hydrolyzate) were added 0.5 ml (excess) of an aqueous suspension of $Cu(OH)_2$ and 0.5 ml of 2% NaOH with stirring and the solution diluted to 10 ml with water. The control (without protein) was prepared in the same order. The solution was kept at room temperature for 3 hours and then centrifuged. The light-absorption curves were plotted on an SF-17 spectrophotometer. The results obtained are presented in Fig. 4.

8. Copper Numbers (number of grams of protein combining with 1 g-atom of Cu). 0.2 g of the substance investigated was dissolved in 25 ml of 2% NaOH and 10 ml of 2% $CuCl_2$. 10 ml of the centrifuged solution was digested by the Kjeldahl method in a mixture of 3 ml of conc. H_2SO_4 and 0.1 g of K_2SO_4, the mixture diluted to 50 ml with water and the copper determined iodometrically. The copper number of the plastein from casein was 603 g and of the plastein from albumin, 496 g. The original proteins had the following copper numbers [20]: casein 568 and albumin 458.

DISCUSSION OF RESULTS

As was established previously and as our investigations showed, plasteins differed very considerably from the mother proteins in many properties. The presence of cyclic forms of links in the plasteins was indicated by the fact that they were not similar to the amino acid polymers obtained by the action of enzymes. In this respect it is quite evident that they were not similar to the quasi-proteinssynthesized by Bresler et al. [13] by the action of enzymes on enzyme protein hydrolyzates at high pressure. Plasteins are peculiar proteinaceous substances, namely amino acid anhydrides with a peptido-piperazine structure. The greatest peculiarity of these substances appeared, for example, in experiments on animals [22]. On internal administration, the plastein from casein showed an incomparably greater toxic action than its mother protein. It is interesting to note that during hydrolysis with boiling water, the plastein lost its toxic properties.

From our investigations we can surmise the following as regards the mechanism of plastein synthesis. As was established [26], in the initial stage of hydrolysis protein is depolymerized and broken down into relatively coarse particles, monomers, which undergo further hydrolysis to lose a certain amount of cyclic anhydrides and are converted into piperazine peptides with a molecular weight of about 1000. Considering the peculiarity of the properties of plasteins and their low molecular weight [12], it can be considered that in plastein formation from piperazine peptides the hydrolyzate under enzyme action,plastein monomers are synthesized with a smaller number of cyclic anhydrides and longer peptide chains than in the original protein. This apparently explains the observed lower nitrogen content of the plasteins than that of the mother proteins. A difference of approximately 1% (of the 15-16% total nitrogen of the mother proteins) represents about 6% nitrogen of the rings eliminated during hydrolysis. The monomers then undergo relatively slight polymerization, which then completes the formation of the plasteins, which are insoluble in water, have a low molecular weight (about 6000), are more acid than the mother proteins, are electrophoretically homogeneous and lack the specific properties of proteinaceous materials. If in plasteins there exists one of the microstructures of protein, proposed by one of us [27], the formation of a plastein of this structure may be explained by the elimination from that part of the diketopiperazine that is surrounded by a dotted line in the scheme.



SUMMARY

1. Plasteins were synthesized by Danilevskii's method from enzyme and acid hydrolyzates of two varieties of casein and human serum albumin. Their properties were characterized by electrophoresis, electroreduction, spectrophotometry and determination of the copper and titration numbers.

2. The plasteins differed considerably in their properties from the mother proteins. The proteinlike substances, plasteins, are comparatively low-molecular weight, electrophoretically homogeneous amino acid anhydrides with a peptido-cyclic structure, having longer peptide chains and a smaller number of cyclic forms of amino acid links than the original proteins.

3. The synthesis of plasteins is not a simple reversal of the hydrolysis reaction. The hydrolysis and subsequent synthesis is accompanied by considerable rearrangement of the protein structure. The peculiarity of the properties of plasteins is the result of this rearrangement.

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ALLYL ESTERS OF SOME ALKANE-, ALKENE- AND CHLORO-ALKANEPHOSPHINIC ACIDS

L. Z. Soborovskii and Yu. M. Zinov'ev

Allyl esters of alkanephosphinic acids have a certain value as starting materials for the preparation of polymeric materials. Esters of various alkane- and alkenephosphinic acids were obtained by the action of allyl alcohol on the acid chlorides of appropriate phosphinic acids [1, 2] or by the Arbuzov method from triallyl phosphite and alkyl halides [3]. The allyl ester of octanephosphinic acid was obtained by the reaction of the free acid and allyl alcohol in boiling toluene in the presence of 1.3% of para-toluenesulfonic acid [4]. Kamai and Kukhtin [5] and also Toy and Ratenberg [6] described allyl esters of chloroalkanephosphinic acids.

In the present work we synthesized allyl esters of certain alkane-, alkene- and chloroalkanephosphinic acids, starting from the diacid chlorides of the appropriate acids, obtained by oxidative chlorophosphination of paraffin and olefin hydrocarbons (heptane, cyclohexane, propylene and butene-1).

Since certain diacid chlorides obtainable by this method are mixtures of isomeric compounds, then the esters synthesized from them also consist of isomers, differing in the position of the phosphorus-containing residue in the hydrocarbon radical [7, 8].

In addition, dehydrochlorination of the acid chloride of chloropropanephosphinic acid yielded the acid chloride of propenephosphinic acid, which was then converted into the allyl ester of propenephosphinic acid (the latter may have contained traces of isomeric compounds).

The properties of the compounds synthesized are presented in the table.

EXPERIMENTAL

1. Diallyl Heptanephosphinate (I). Over a period of 2.5 hours, 36.1 g (0.165 mole) of heptanephosphinyl chloride [7] was added to a mixture of 19.3 g (0.33 mole) of allyl alcohol and 26.3 g (0.33 mole) of pyridine at 0-5°. After 1 hour, 10 ml of water was added to the reaction mixture and the organic layer separated, washed with 3% NaOH solution in 10% NaCl solution, dried in vacuum (3 mm) with heating on a water bath and vacuum distilled. We isolated 14.1 g of material.

Found %: C 59.26, 59.09; H 9.03, 9.24. $C_{13}H_{25}O_3P$. Calculated %: C 59.95; H 9.60.

2. Diallyl Cyclohexanephosphinate (II). Under the conditions of experiment 1, from 19.3 g (0.33 mole) of allyl alcohol and 33.5 g (0.165 mole) of cyclohexanephosphinyl chloride [7] we obtained 8.9 g of material.

Found %: C 58.30, 58.26; H 9.37, 9.56. $C_{12}H_{21}O_3P$. Calculated %: C 58.98; H 8.65.

3. Diallyl Chloropropanephosphinate (III). At 5° 97.7 g (0.5 mole) of chloropropanephosphinyl chloride was gradually added to a mixture of equimolecular amounts of allyl alcohol (58.0 g) and triethylamine (101 g), dissolved in twice the volume of benzene. The precipitate of triethylamine hydrochloride was removed, the benzene distilled from the filtrate and the residue vacuum distilled. We isolated 72 g of material.

Found %: C 45.22, 44.90; H 6.17, 6.35; P 13.73, 13.66. $C_9H_{16}O_3ClP$. Calculated %: C 45.27; H 6.76; P 12.98.

4. Diallyl Chlorobutanephosphinate (IV). Under the conditions of experiment 3, from 21.0 g (0.1 mole) of chlorobutanephosphinyl chloride (mixture of isomers formed by oxidative chlorophosphination of butene-1 [7, 8]) and 12.0 g (0.2 mole) of allyl alcohol we isolated 4.7 g of (IV).

Compound	Formula	Boiling point (pressure in mm)	d_4^{20}	n_D^{20}	MR_D found	MR_D calculated	Yield (in %)
(I)	$C_7H_{15}P(O)(OC_3H_5)_2$*	117—123° (3)	0.9986	—	—	—	32.7
(II)	$C_6H_{11}P(O)(OC_3H_5)_2$**	130 (4)	1.0549	—	—	—	22
(III)	$C_3H_6ClP(O)(OC_3H_5)_2$*	113—115 (3)	1.122	1.4598	59.2	58.6	60
(IV)	$C_4H_8ClP(O)(OC_3H_5)_2$*	117—118 (3)	1.0980	1.4618	63.2	63.22	18.6
(V)	$C_3H_5P(O)(OC_3H_5)_2$***	98 (3.5)	1.0375	1.4558	53.0	53.23	54.6
(VI)	$C_3H_5P(O)Cl_2$	75—77 (16)	1.3343	1.4815	33.9	33.65	50.7

*Mixtures of isomers.

**The substance has been described. According to Toy and Cooper [1] it has b.p. 100-103° (0.5 mm), d_4^{20} 1.0485, $n^{20}D$ 1.4734. Castro and Elwell [2] report data close to those we found.

***The diallyl ester of allylphosphinic acid obtained by other method [5] boiled at 94-95° (3 mm), d_4^{20} 1.0050, $n^{20}D$ 1.4600.

Found %: C 46.65, 47.02; H 5.93, 6.42. $C_{10}H_{18}O_3ClP$. Calculated %: C 47.5; H 7.1.

5. Dehydrochlorination of Chloropropanephosphinyl Chloride. Through a glass tube filled with activated charcoal at 250-300° was passed the vapor of chloropropanephosphinyl chloride. The system was maintained at a residual pressure of 50 mm. The liquid draining into the receiver yielded propenephosphinyl chloride (VI).

Found %: Cl 44.7, 44.9. $C_3H_5OCl_2P$. Calculated %: Cl 44.9.

6. Diallyl Propenephosphinate (V). 16.4 g (0.106 mole) of (VI) was added at -15° to a 6-fold amount of allyl alcohol. The reaction mixture was neutralized with calcined soda, the precipitate of salts removed, the excess allyl alcohol distilled off and the residue vacuum distilled. We isolated 11.7 g of material.

Found %: C 53.70, 53.40; H 7.90, 8.15. $C_9H_{15}O_3P$. Calculated %: C 53.46; H 7.42.

SUMMARY

1. For the preparation of diallyl esters of alkane- and substituted alkanephosphinic acids we used the acid chlorides of these acids, formed by oxidative chlorophosphination of appropriate hydrocarbons or their derivatives.

2. The diallyl esters of heptane-, cyclohexane-, chloropropane-, chlorobutane- and propenephosphinic acids were synthesized.

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SYNTHESIS OF TRIALKYLGERMANIUM FLUORIDES

B. M. Gladshtein, V. V. Rodé and L. Z. Soborovskii

Trialkylgermanium fluorides were obtained previously by replacement of the halogen atom by fluorine in trialkylgermanium monohalides [1] and also by cleavage of hexaalkyldigermoxanes with hydrogen fluoride [2].

The action of hydrogen halides on tetramethylgermanium was studied by Dennis and his co-workers. The authors found that concentrated hydrochloric acid did not react with tetramethylgermanium in the cold [3] and that gaseous hydrogen bromide removed a methyl group from tetramethylgermanium only under the catalytic action of anhydrous aluminum bromide [4].

In the present work a method was found for preparing trialkylgermanium fluoride by the direct action of liquid hydrogen fluoride on tetraalkylgermanium:

$$GeR_4 + HF \rightarrow R_3GeF + RH, \text{ where } R = CH_3 \text{ and } C_2H_5$$

The reaction proceeded smoothly under mild conditions and led to a quantitative yield of trialkylgermanium monofluoride. It is possible that this reaction could be used for developing a quantitative method of determining some tetraalkylgermaniums.

The replacement of one alkyl group by fluorine in tetraalkylgermanium had a noticeable effect on the properties of the remaining Ge—C bonds. Further action of hydrogen fluoride on trialkylgermanium fluorides, even under more drastic conditions, did not lead to removal of the next alkyl groups. Thus, this method makes it possible to synthesize trialkylgermanium fluorides in a pure form without traces of alkylgermanium di- and trifluorides, which makes the method found convenient from the preparative point of view.

The values of the atomic refraction increments of germanium for trimethyl- and triethylgermanium fluorides varied insignificantly (8.35 and 8.28, respectively).

The starting tetraalkylgermaniums were prepared by organomagnesium synthesis from germanium tetrachloride and the appropriate alkylmagnesium halide. The preparation of tetramethylgermanium by this method in dibutyl ether under the conditions we found led to a practically quantitative yield. It should be noted that dibutyl ether was used previously for the synthesis of tetraalkylgermaniums [5], but the yield of the latter was insignificant under the conditions used by the authors.

EXPERIMENTAL

Tetramethylgermanium. A solution (1 : 1) of 26.8 g of germanium tetrachloride in absolute dibutyl ether was added dropwise to methylmagnesium bromide (from 24 g of magnesium and 105-110 g of methyl bromide) in 300 ml of absolute dibutyl ether with cooling to -10 to -15°. The reaction mixture was heated for 8 hours on a boiling water bath. It was decomposed on cooling with ice-water and then concentrated sulfuric acid was added until the precipitate dissolved completely. The ternary mixture of tetramethylgermanium, dibutyl ether and water was distilled from the reaction mixture at a temperature of up to 95°. The ether layer was separated, dried with anhydrous sodium sulfate and separated on a fractionating column. The yield was 15.5 g (95%).

B.p. 42.5-43.0° (753 mm), $n^{20}D$ 1.3871, d_4^{20} 1.0064. Literature data: b.p. 42.2° (710 mm) [7], 43.2° (760 mm) [3], 43.4° [6], $n^{23.5}D$ 1.3868, d^0 1.003, 1.009 [3].

Trimethylgermanium Fluoride. Into a copper cylinder cooled with solid carbon dioxide and fitted with a copper reflux condenser was placed 13 g of tetramethylgermanium, and 10 g of hydrogen fluoride was quickly poured in. The reaction began at a temperature of -10 to -15° and was almost complete at 20-25°. For completion, the reaction mixture was heated for 2-3 hours on a water bath at 50-55°. The end of the reaction was determined by cessation of gas evolution, the latter being collected in a gasometer. For removal of excess hydrogen fluoride, the reaction mixture was treated with anhydrous potassium fluoride, decanted and distilled. The yield was 9.6 g (71%).

B.p. 77-78° (755 mm), $n^{20}D$ 1.3855, d_4^{20} 1.2114, MR_D 26.51; calc. 18.16. AR_{Ge} 8.35.

Found %: C 26.82, 27.33; H 6.74, 6.79; F 13.69, 14.16. C_3H_9FGe. Calculated %: C 26.34; H 6.57; F 13.81.

Literature data: b.p. 76° (746 mm), $n^{20}D$ 1.3863, d_4^{20} 1.2300 [1].

The gas collected in the gasometer (95% yield) was condensed and its molecular weight determined.

Found: MW 16.57, 18.62. CH_4. Calc. MW 16.04.

Triethylgermanium Fluoride. In a similar way, from 10 g of tetraethylgermanium* and 6 g of hydrogen fluoride we obtained 6.5 g (71%) of triethylgermanium fluoride. The reaction began at 10-15°. Over a period of 5 hours, the temperature in the water bath was raised to 75-80°. The reaction mixture was treated analogously.

B.p. 147-148° (744 mm), $n^{20}D$ 1.4206, d_4^{20} 1.1527, MR_D 39.30; calc. 31.02. AR_{Ge} 8.28.

Literature data: b.p. 149.0° (751 mm) [2].

Ethane (95% yield) was collected in the gasometer.

Found: MW 30.63, 31.15. C_2H_6 Calc. MW 30.07.

SUMMARY

1. A method was found for synthesizing trialkylgermanium fluorides by the action of hydrogen fluoride on tetraalkylgermaniums.

2. It was shown that tetramethylgermanium could be obtained in high yield by organomagnesium synthesis in dibutyl ether under the conditions found.

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NEW ESTERS OF N-TRIFLUOROMETHYLCARBAMIC ACID

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According to literature data fluorinated alkyl isocyanates have a high reactivity [1]. In particular, they react readily with alcohols and phenols with the formation of esters of N-perfluoroalkylcarbamic acid.

$$R_FNCO \xrightarrow{CH_3OH} R_FNHCO_2CH_3$$

In previous communications [2] we described the reactions of trifluoromethyl isocyanate with hydrohalic acids and with mercaptans. Since the study of the chemical properties of alkyl isocyanates and their fluorinated derivatives is of definite interest, in the present communication we describe the preparation of certain new esters of N-trifluoromethylcarbamic acid. The constants and analytical data for the new compounds prepared are presented in the table.

EXPERIMENTAL

Trifluoromethyl isocyanate reacted with the usual alcohols with strong evolution of heat. Therefore, for the most part we reacted equimolecular amounts of trifluoromethyl isocyanate and alcohol in a sealed glass ampule, which was periodically cooled by immersion in a cooling mixture of acetone and solid carbon dioxide (or in liquid nitrogen). The ampule was then opened and the reaction products distilled under reduced pressure. The yield of pure product was not less than 55% and in separate cases it was 70-85%.

As examples we describe only those experiments on the preparation of N-trifluoromethylcarbamates, which are typical.

Ethyl N-trifluoromethylcarbamate. Into a glass ampule of 30 ml capacity was placed 2.8 g (0.06 mole) of alcohol and with cooling in liquid nitrogen, 7 g (0.063 mole) of trifluoromethyl isocyanate was added. After being sealed, the ampule was heated to room temperature, when the reaction proceeded vigorously and required periodic cooling of the ampule. The ampules were opened and the crystals obtained were distilled under reduced pressure. The yield was 8.0 g (84%).

β-Cyanoethyl N-trifluoromethylcarbamate. Into a glass ampule of 30 ml capacity was placed 2.4 g (0.033 mole) of ethylene cyanhydrin and 4 g (0.036 mole) of trifluoromethyl isocyanate was added with the ampule cooled with liquid nitrogen. After being sealed, the ampule was heated to room temperature; thereupon two layers of liquid formed. When shaken, the contents of the ampule heated up moderately and crystallized. At the end of the reaction, the ampule was opened and the solid crystalline substance extracted. The yield was 4 g (66%).

1,1,3-Trihydroperfluorobutyl N-trifluoromethylcarbamate. Into a glass ampule of 30 ml capacity was placed 5.5 g (0.03 mole) of 1,1,3-trihydroperfluorobutyl alcohol, and 3.5 g (0.031 mole) of trifluoromethyl isocyanate was added with the ampule cooled in liquid nitrogen. After being sealed, the ampule was heated to room temperature, when the reaction proceeded for days without evolution of heat. The ampule was opened and the contents distilled under reduced pressure. The yield was 6.5 g (73%).

Phenyl N-trifluoromethylcarbamate. Into a glass ampule of 30 ml capacity was placed 2.3 g (0.024 mole) of phenol, dissolved in 3 ml of dry ethyl ether, and 3 g (0.027 mole) of trifluoromethyl isocyanate was added with the ampule cooled in liquid nitrogen. After being sealed, the ampule was heated to room temperature, when the

Substance	Melting point	Boiling point (pressure in mm)	d_4^t	n_D^t	MR_D		% N		% F	
					calc.	found	calc.	found	calc.	found
$CF_3NHCO_2C_2H_5$	28°	52° (7)	1.2946 (30°)	1.3470 (30°)	25.91	25.89	8.91	9.14	36.30	36.36
$CF_3NHCO_2CH_2CH_2CH_3$	—	90 (42)	1.2488 (20)	1.3658 (20)	30.53	30.65	8.18	8.20	33.33	33.40
$CF_3NHCO_2CH(CH_3)_2$	41	53 (7)	—	—	—	—	8.18	8.91	33.33	33.38
$CF_3NHCO_2CH_2CH=CH_2$	—	89 (41)	1.2924 (20)	1.3760 (20)	30.07	30.00	8.28	8.25	33.72	33.61
$CF_3NHCO_2CH_2COCH_3$	64	110 (5)	—	—	—	—	7.56	7.41	30.81	30,81
$CF_3NHCO_2CH_2CH_2CH_2CH_3$	—	78 (10)	1.2027 (20)	1.3730 (20)	35.15	35.04	7.56	7.48	30.81	30.77
$CF_3NHCO_2CH_2CH_2CH(CH_3)_2$	—	78 (6)	1.1643 (21)	1.3810 (20)	39.77	39.68	7.03	7.05	28.64	28.70
$CF_3NHCO_2CHCH_3CH(CH_3)_2$	—	65 (4)	1.1627 (21)	1.3800 (21)	39.77	39.64	7.03	7.19	28.64	28.41
$CF_3NHCO_2CHCH_3C(CH_3)_3$	54.5	80 (6)	—	—	—	—	6.57	7.05	26.76	26.58
$CF_3NHCO_2CH_2CH_2C(CH_3)_3$	—	93 (12)	1.1360 (20)	1.3904 (20)	44.39	44.47	6.57	6.64	26.76	26.56
$CF_3NHCO_2C_6H_5$	88	124 (47)	—	—	—	—	6.82	7.18	27.80	27.80
$CF_3NHCO_2CH_2CN$	44	100 (3)	—	—	—	—	16.66	16.44	33.92	34.63
$CF_3NHCO_2CH_2CH_2CN$	84	—	—	—	—	—	15.38	14.90	31.31	31.29
$CF_3NHCO_2CH_2CH_2NO_2$	58	125 (6)	—	—	—	—	13.86	13.71	28.21	28.19
$CF_3NHCO_2CH_2CH_2Br$	61	91 (10)	—	—	—	—	—	—	24.15	24.08
$CF_3NHCO_2CH_2CH_2Cl$	48.5	82 (7)	—	—	—	—	7.31	7.60	29.76	29.52
$CF_3NHCO_2CH_2CH_2CF_3$	31	59 (60)	—	—	—	—	6.22	6.57	50.66	50.18
$CF_3NHCO_2CH_2CF_2CHFCF_3$	—	84 (15)	1.6467 (21)	1.3275 (21)	36.05	36.09	4.77	5.08	57.28	57.41
$CF_3NHCO_2C(CH_3)_2C\equiv CCF_3$	75	77 (8)	—	—	—	—	5.32	5.58	43.34	43.47
$CF_3NHCO_2CH_2CH_2SCH_2CH_3$	34	116 (8)	—	—	—	—	8.45	8.49	26.26	26.34
$CF_3NHCO_2CH_2CH_2SCH_2CH(CH_3)_2$	—	112 (3)	1.2148 (17)	1.4370 (17)	52.46	52.83	5.71	5.67	23.26	23·60

reaction proceeded for days without the evolution of heat. The ampule was opened, the ether removed and the product distilled under reduced pressure. The yield was 4.5 g (84%).

SUMMARY

A series of new esters of N-trifluoromethylcarbamic acid were synthesized.

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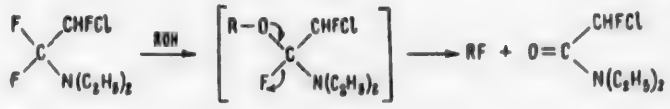
*Original Russian pagination. See C. B. Translation.

FLUORINATION BY MEANS OF α-FLUORINATED AMINES

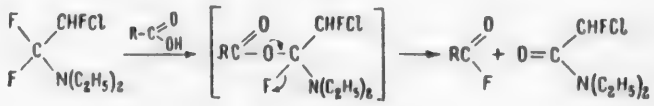
N. N. Yarovenko and M. A. Raksha

By studying the chemical properties of α-fluorinated amines we found new methods of preparing fluoro-organic compounds.

As we established, α-fluorinated amines of the type RCF_2NR_2' react with alcohols with the formation of alkyl fluorides. The reaction proceeded very readily on simple mixing of the reagents, with alkyl fluoride yields of up to 66%.



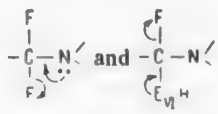
Fluorinated amines of the type RCF_2NR_2 reacted analogously with carboxylic acids, their salts and thiocarboxylic acids with the formation of acid fluorides of carboxylic acids.



As is known, the hydrolysis of α-fluorinated amines yields substituted amides of fluorinated carboxylic acids [1, 2]. The reactions of α-fluorinated amines with hydrogen sulfide and hydrogen selenide proceeded similarly. This formed the previously unknown dialkylamides of fluorinated thiocarboxylic and selenocarboxylic acids.

$$CHFClCF_2N(C_2H_5)_2 \xrightarrow{H_2S} CHFClCSN(C_2H_5)_2$$
$$CHF_2CF_2N(C_2H_5)_2 \xrightarrow{H_2S} CHF_2CSN(C_2H_5)_2$$
$$CHF_2CF_2N(C_2H_5)_2 \xrightarrow{H_2Se} CHF_2CSeN(C_2H_5)_2$$

The great lability of fluorine atoms in an α-position to nitrogen and the ease with which they replace elements of group 6 may be explained by pσ-conjugation [4].



E – element

The fluorinated amines required for these reactions were obtained by the reaction of secondary amines with fluorinated olefins [2, 3]. Secondary amines added to trifluorochloroethylene particularly readily (as we showed, on simply bubbling trifluorochloroethylene through diethylamine).

$$CF_2{=}CFCl \xrightarrow{HN(C_2H_5)_2} CHFClCF_2N(C_2H)_2$$

All the reactions described in this work could be carried out in normal glass apparatus.

EXPERIMENTAL

1,1,2,2-Tetrafluoroethyldimethylamine. Into a glass ampule of 250 ml capacity were placed 4.5 g (0.1 mole) of dimethylamine and 10.0 g (0.1 mole) of tetrafluoroethylene with cooling. The ampule was sealed, placed in a beaker with carbon dioxide and acetone, cooled to -70° and left for 15 hours, when the mixture was gradually heated to room temperature. The ampule was then opened and the reaction products distilled. The yield was 11.8 g (81%). The b.p. was 32° (127 mm). The colorless liquid fumed strongly in air.

Found %: F 52.10. $C_4H_7NF_4$. Calculated %: F 52.41.

Dimethylamide of Difluoroacetic Acid. 7.5 g (0.051 mole) of 1,1,2,2-tetrafluoroethyldimethylamine was poured in small portions from a dropping funnel with cooling and stirring into a beaker with 4.7 g of crushed ice. To the liquid obtained was added 10 ml of ether and the ether solution separated, dried with sodium sulfate and distilled. The yield was 5.5 g (95%). In contrast to the diethylamide of difluoroacetic acid, the product dissolved in water very readily.

B.p. 61° (29 mm), $n^{20}D$ 1.4012, d_4^{20} 1.2150.

Found %: F 30.51. $C_4H_7ONF_2$. Calculated %: F 30.82.

2-Chloro-1,1,2-trifluorotriethylamine. In a Drechsel bottle, cooled to -5 to -10°, was placed 40.0 g (0.56 mole) of diethylamine and over a period of 10 hours 70.0 g (0.06 mole) of well dried trifluorochloroethylene was bubbled through it. The reaction mixture was then distilled under reduced pressure. The yield was 70.0 g (61%). The b.p. was 33° (6 mm). According to data in [2]: b.p. 32-33° (6 mm).

Dimethylamide of Difluoroselenoacetic Acid. In a Drechsel bottle fitted with a thermometer was placed 14.5 g (0.1 mole) of 1,1,2,2-tetrafluoroethyldimethylamine, which was heated to 40° and into it was bubbled 9 g (0.11 mole) of hydrogen selenide (obtained by the reaction of aluminum selenide with water). The reaction mixture heated up to 70-100°. The color of the liquid gradually became orange. When slightly more than half of the calculated amount of hydrogen selenide had been absorbed, the evolution of hydrogen fluoride began and elementary selenium was partially liberated. The contents were poured into water and the oil was separated, dried with sodium sulfate and distilled. The yield was 3.6 g (19.3%). The orange liquid had a nauseating odor. It dissolved readily in the usual organic solvents. It was insoluble in water.

B.p. 84° (11 mm), $n^{20}D$ 1.5460, d_4^{20} 1.5405.

Found %: Se 42.36; F 20.47. $C_4H_7NF_2Se$. Calculated %: Se 42.45; F 20.43.

Diethylamide of Difluoroselenoacetic Acid. Under analogous conditions from 17.3 g (0.1 mole) of 1,1,2,2-tetrafluorotriethylamine and 9.5 g (0.12 mole) of hydrogen selenide we obtained 8.0 g (37.5%) of the diethylamide.

B.p. 83° (7 mm), $n^{20}D$ 1.5360, d_4^{20} 1.4306.

Found %: C 34.09; H 5.35; N 6.61; Sc 36.29; F 17.78. $C_6H_{11}NF_2Se$. Calculated %: C 33.66; H 5.18; N 6.54; Se 36.88; F 17.75.

Dimethylamide of Difluorothioacetic Acid. From 14.5 g (0.1 mole) of 1,1,2,2-tetrafluoroethyldimethylamine and 4.0g (0.12 mole) of hydrogen sulfide we obtained 3.4 g of the dimethylamide. The liquid had a light yellow color. The smell was unpleasant. The product dissolved readily in the usual organic solvents. It was insoluble in water.

B.p. 83° (33 mm), $n^{20}D$ 1.5070, d_4^{20} 1.2480.

Found %: S 23.08; F 27.63. $C_4H_7NSF_2$. Calculated %: S 23.04; F 27.03.

Diethylamide of Difluorothioacetic Acid. From 17.3 g (0.1 mole) of 1,1,2,2-tetrafluorotriethylamine and 4.7 g (0.14 mole) of hydrogen sulfide we obtained 9.2 g (55%) of the diethylamide of difluorothioacetic acid.

B.p. 66° (6 mm), $n^{20}D$ 1.4752, d_4^{20} 1.1346.

Found %: C 42.68; H 6.67; N 8.14; S 18.94; F 22.63. $C_6H_{11}NSF_2$. Calculated %: C 43.11; H 6.58; N 8.38; S 19.16; F 22.75.

Diethylamide of Fluorochlorothioacetic Acid. In a Drechsel bottle fitted with a thermometer was placed 18.95 g (0.1 mole) of 2-chloro-1,1,2-trifluorotriethylamine, which was heated to 40° and 3.4 g (0.107 mole) of hydrogen sulfide bubbled through it. The reaction mixture heated to 70-80°. It was washed twice with ice water and then with 2% sodium bicarbonate solution, dried with sodium sulfate and distilled. The yield was 4.3 g (23.5%).

B.p. 98° (8 mm), $n^{20}D$ 1.5175, d_4^{20} 1.1954.

Found %: S 17.38; F 10.72; Cl 19.40. $C_6H_{11}NSFCl$. Calculated %: S 17.47; F 10.35; Cl 19.33.

Fluorination of Acetic Acid. 12.0 g (0.2 mole) of acetic acid was added dropwise to 37.8 g (0.2 mole) of 2-chloro-1,1,2-trifluorotriethylamine. The gases liberated were passed through a glass tube filled with calcinedpotassium fluoride and trapped in a receiver at -70°. The gaseous reaction products were then distilled. The yield of acetyl fluoride was 7.3 g (59%).

B.p. 20.5° (752 mm). According to data [5]: b.p. 21-22°.

Found %: F 30.3. C_2H_3OF. Calculated %: F 30.62.

The liquid remaining in the reaction flask yielded 23.4 g (69%) of the diethylamide of fluorochloroacetic acid.

B.p. 105° (27 mm), $n^{20}D$ 1.4490. According to data [2]: b.p. 47° (0.7 mm), $n^{25}D$ 1.4499.

Fluorination of Thioacetic Acid. Under conditions analogous to those of the previous experiment, from 15.2 g (0.2 mole) of thioacetic acid and 37.8 g (0.2 mole) of 2-chloro-1,1,2-trifluorotriethylamine we obtained 6.2 g (50%) of acetyl fluoride. The b.p. was 21°. According to data in [5] the b.p. 21-22°. The liquid remaining in the flask was washed with water, dried with sodium sulfate and distilled. We obtained 21.7 g (60%) of the diethylamide of fluorochlorothioacetic acid.

B.p. 98° (8 mm), $n^{20}D$ 1.5175.

Found %: Cl 19.21. $C_6H_{11}NSFCl$. Calculated %: Cl 19.33.

Fluorination of Propionic Acid. 14.8 g (0.2 mole) of propionic acid was added dropwise to 37.8 g (0.2 mole) of 2-chloro-1,1,2-trifluorotriethylamine. The reaction mixture evolved heat and the propionyl fluoride partially distilled. The mixture was heated on a water bath to complete the reaction. The liquid obtained was distilled. The yield of propionyl fluoride was 6.1 g (40%).

B.p. 44°. According to data [5]: b.p. 44°.

Found %: F 25.63. C_3H_5OF. Calculated %: F 25.0.

The liquid remained in the reaction flask yielded 24.3 g (73%) of the diethylamide of fluorochloroacetic acid.

B.p. 105° (27 mm), $n^{20.5}D$ 1.4496. According to data [2]: b.p. 47° (0.7 mm), $n^{25}D$ 1.4499.

Fluorination of Sodium Propionate. 5.85 g (0.1 mole) of sodium propionate was added from a hermetically attached flask to 18.9 g (0.1 mole) of 2-chloro-1,1,2-trifluorotriethylamine. The reaction mixture evolved heat and propionyl fluoride distilled. The yield was 4.0 g (87%). The b.p. was 44° and the $n^{13}D$ 1.3290. According to data in [2], the b.p. is 44°. The liquid remaining in the reaction flask yielded 7.8 g of the diethylamide of fluorochloroacetic acid.

B.p. 105° (27 mm), $n^{20}D$ 1.4496. According to data in [2]: b.p. 47° (0.7 mole), $n^{25}D$ 1.4499.

Fluorination of Butyric Acid. Under conditions analogous to those for the preparation of propionyl fluoride, from 37.8 g (0.2 mole) of 2-chloro-1,1,2-trifluorotriethylamine and 17.6 g (0.2 mole) of butyric acid we obtained 8.2 g (45.5%) of butyryl fluoride.

B.p. 67°, $n^{20}D$ 1.3470. According to data [5]: b.p. 67°, $n^{15.5}D$ 1.3487.

Found %: F 21.51. C_4H_7OF. Calculated %: F 21.08.

1-Fluorobutane. 14.8 g (0.2 mole) of n-butyl alcohol was added dropwise to 37.8 g (0.2 mole) of 2-chloro-1,1,2-trifluorotriethylamine. The reaction mixture evolved heat and a low-boiling liquid distilled. The liquid obtained was washed with ice-water, dried with calcium chloride and distilled. The yield was 10.1 g (66.5%).

B.p. 31.5° (731 mm), $n^{20}D$ 1.3410.

Found %: F 25.10. C_4H_9F. Calculated %: F 25.0.

The liquid remaining in the flask yielded 24.3 g (72.5%) of the diethylamide of fluorochloroacetic acid.

B.p. 105° (27 mm), $n^{20}D$ 1.4490. According to data [2]: b.p. 47° (0.7 mm), $n^{20}D$ 1.4499.

1-Fluoro-3-methylbutane. Under conditions analogous to those of the previous experiment, from 37.8 g (0.2 mole) of 2-chloro-1,1,2-trifluorotriethylamine and 17.6 g (0.2 mole) of isoamyl alcohol we obtained 6.3 g (35%) of 1-fluoro-3-methylbutane.

B.p. 53.5°, $n^{18}D$ 1.3612. According to data [6]: b.p. 53.2°.

Found %: F 21.11. $C_5H_{11}F$. Calculated %: F 21.07.

The liquid remaining in the reaction flask yielded 18.6 g (55.5%) of the diethylamide of fluorochloroacetic acid.

B.p. 105° (27 mm), $n^{20}D$ 1.4490. According to data [2]: b.p. 47° (0.7 mm), $n^{25}D$ 1.4499.

SUMMARY

1. A new preparative method was described for obtaining acid fluorides of carboxylic acids and alkyl fluorides by replacing hydroxyl or sulfhydryl groups by fluorine with the help of α-fluorinated tertiary amines.

2. A method was found for preparing substituted amides of fluorinated thiocarboxylic and selenocarboxylic acids.

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DIFLUOROCHLOROMETHYLSULFENYL CHLORIDE

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Up to now no methods were known for the preparation of mixed compounds of the difluorochloro- or difluorobromomethylsulfenyl halide type.

As is known, trifluoromethylsulfenyl chloride is obtained by ultraviolet irradiation of a mixture of hexafluorodimethyl sulfide with chlorine at room temperature [1].

$$CF_3SSCF_3 \xrightarrow{Cl_2} CF_3SCl$$

The hexafluorodimethyl disulfide required for this reaction was obtained by reacting trifluoroiodomethane with sulfur [2]. Trifluoromethylsulfenyl chloride was also formed by the reaction of mercury trifluoromethylmercaptide with chlorine [1].

$$(CF_3S)_2Hg \xrightarrow{Cl_2} CF_3SCl + CF_3SHgCl$$

However it was impossible to obtain difluorohalomethylsulfenyl halides of the type CF_2XSX by this method or by the other usual reactions. The C – S bond is broken during the reaction of trichloromethylsulfenyl chloride with metal fluorides. In the reaction of carbon disulfide with hydrogen fluoride and chlorine or with antimony fluorides in the presence of antimony pentachloride and also with fluorides of certain other elements all the C – S bonds are broken and fluorochloromethanes are formed [3].

The object of the present work was to find a method of synthesizing difluorochloromethylsulfenyl chloride.

In contrast to trichloromethylsulfenyl chloride, the product of its interaction with diethylamine, trichloromethyl-(N-diethyl)-sulfenamide, reacted with antimony trifluoride in the presence of small amounts of antimony pentachloride under mild conditions without rupture of the C – S bond with the formation of fluorodichloro-, difluorochloro- and, apparently, trifluoromethyl-(N-diethyl)-sulfenamides. The reaction was found to be very sensitive to temperature and heating time. At temperatures below 65° practically only fluorodichloromethyl-(N-diethyl)-sulfenamide was formed. At 67° and with an hour and a half's heating, difluorochloromethyl-(N-diethyl)-sulfenamide was obtained in a yield of about 25% in a mixture with fluorodichloro- and trichloromethyl-(N-diethyl)-sulfenamide. In view of the instability of difluorochloromethyl-(N-diethyl)-sulfenamide, there was no need to isolate it from the reaction mixture in a pure form. It was sufficient to separate the mobile liquid from the solid and tarry reaction products and to saturate it with dry hydrogen chloride [4].

$$CCl_3SN(C_2H_5)_2 \xrightarrow{SbF_3+SbCl_5} CF_2ClSN(C_2H_5)_2 + CFCl_2SN(C_2H_5)_2 + CCl_3SN(C_2H_5)_2 \xrightarrow{HCl}$$
$$\longrightarrow CF_2ClSCl + CFCl_2SCl + CCl_3SCl$$

The mixture of trichloro-, difluorochloro- and fluorodichloromethylsulfenyl chlorides obtained in this way were readily separated by distillation on a column. The effect of temperature and heating time on the yield of difluorochloro- and fluorodichloromethylsulfenyl chlorides is shown in the table.

EXPERIMENTAL

Difluorochloromethylsulfenyl Chloride. Into a three-necked glass flask of 0.5 liter capacity, fitted with a stirrer and thermometer, were placed 200 g (0.9 mole) of trichloromethyl-(N-diethyl)-sulfenamide, 120 g

Reagent	Experiment 1	Experiment 2	Experiment 3
$CCl_3SN(C_2H_5)_2$	200 g	200 g	200 g
SbF_3	90	120	120
$SbCl_5$	4	4	4
Temperature in reactor	55°	67°	75°
Heating time	1 hr 45 min	1 hr 20 min	1 hr
Yield of CF_2ClSCl	1.0 g (0.7%)	34 g (24.5%)	30 g (21.7%)
Yield of $CFCl_2SCl$	56 g (37%)	32 g (21%)	3 g (2%)

(0.67 mole) of antimony trifluoride and 4 g of antimony pentachloride. (The ether in which trichloromethyl-(N-diethyl)-sulfenamide is normally obtained had to be removed carefully since even small amounts of ether inhibited the fluorination reaction). With vigorous stirring the reaction mixture was heated to 67° and kept at this temperature until the lower layer became quite black and on an average this occurred after 80 minutes heating. The upper layer was then separated from the tars and saturated with hydrogen chloride for several hours with vigorous stirring and cooling with water and ice; the mixture solidified completely, but toward the end of saturation it again liquefied. The reaction mixture was mixed with finely crushed ice and the oily layer quickly separated, dried with calcium chloride and distilled on a column. The boiling points of CF_2ClSCl (49°) and $CFCl_2SCl$ (99°), calculated from the boiling points of CF_2SCl (~0°) and CCl_3SCl (149°), were close to those found. The yield of difluorochloromethylsulfenyl chloride was 34 g (24.8%). The yellow liquid had the characteristic odor of sulfenyl chlorides, b.p. 52° $n^{19}D$ 1.4195, d_4^{19} 1.5344.

Found %: C 7.72; S 21.07; F 24.40; Cl 46.56. CF_2Cl_2S. Calculated %: C 7.84; S 20.92; F 24.8; Cl 46.41.

The yield of fluorodichloromethylsulfenyl chloride was 32 g (21%).

Found %: C 7.12; S 18.81; F 11.27; Cl 62.65. $CFCl_3S$. Calculated %: C 7.08; S 18.88; F 11.21; Cl 62.83.

The total yield of CF_2ClSCl and $CFCl_2SCl$ was 66 g (45.8%).

SUMMARY

1. The effect of temperature and heating time on the reaction of trichloromethyl-sulfenamide with antimony fluorides and chlorides was studied.

2. It was established that by the reaction of hydrogen chloride with the fluorination products of trichloromethyl-(N-diethyl)-sulfenamide it was possible to prepare difluorochloromethylsulfenyl chloride.

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CARBYLAMINE HALIDES

I. ALIPHATIC CARBYLAMINE CHLORIDES

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Aliphatic carbylamine chlorides have been studied very little. Up to now only three representatives of aliphatic carbylamine chlorides have been known and these are ethyl-, β-chloroethyl- and trichloromethylcarbylamine chlorides. The first substance was obtained by chlorination of ethyl isonitrile [1], the second by chlorination of β-chloroethyl isothiocyanate [2] and the third by thermal decomposition of trichloronitrosomethane [3]. As regards the chemical properties of these compounds, there are only general indications on their reactivity.

In this work the previously unknown methylcarbylamine chloride is described, a method for obtaining the intermediate products in the synthesis of trichloromethylcarbylamine chloride was improved and some of the properties of aliphatic carbylamine chlorides were studied.

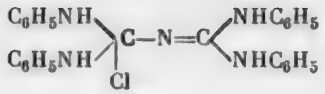
Methylcarbylamine chloride was obtained by chlorination of methyl isothiocyanate in ether at 0°. A characteristic property of methylcarbylamine chloride is its capacity to liberate iodine from acidified solutions of potassium iodide when 1 mole of carbylamine chloride liberates exactly 1 mole of iodine. This property was used for the quantitative determination of methyl-, ethyl- and β-chloroethylcarbylamine chlorides. In the action of potassium iodide on carbylamine chlorides, the replacement of chlorine by iodine apparently occurs first and the carbylamine iodide then decomposes to isonitrile and iodine.

$$R{-}N{=}C\begin{matrix}Cl\\Cl\end{matrix} + 2HI \longrightarrow \left[R{-}N{=}C\begin{matrix}I\\I\end{matrix}\right] + 2HCl$$

$$\left[R{-}N{=}C\begin{matrix}I\\I\end{matrix}\right] \longrightarrow RNC + I_2$$

The isonitriles were not liberated but their presence was detected by odor. In contrast to aliphatic carbylamine chlorides, aromatic ones liberate hardly any iodine from an acidified solution of potassium iodide. Trichloromethylcarbylamine chloride occupies an intermediate position between aliphatic and aromatic compounds in this respect. Thus, when treated with KI for 2 hours, this carbylamine chloride showed a 10.6% content of active chlorine and after 2 days, 19.3% (theoretical content of active chlorine, 33%).

In contrast to aromatic carbylamine chlorides, methyl- and trichloromethylcarbylamine chlorides did not react with hydrogen sulfide (even on heating) or with sodium and copper sulfides in an aqueous medium or in benzene and dioxane solution when heated to 100°. The carbylamine chlorides reacted vigorously with amines. The action of aniline on trichloromethylcarbylamine chloride caused replacement of all the chlorine atoms, even when the reaction was carried out in dilute solutions and with excess carbylamine chloride. The reaction products yielded two substances, which were apparently derivatives of guanidine (I) and (II). According to elementary composition, (I) corresponded to di-(phenylamino)-chloromethyldiphenylguanidine and (II) to tri-(phenylamino)-methyldiphenylguanidine. The substances were not examined more closely.



(I)

$(C_6H_5NH)_3CN{=}C(NHC_6H_5)_2$

(II)

Trichloromethylcarbylamine chloride was obtained from tetrachloromethyl mercaptan by the method described in the literature [3]. This method is extremely complex and certain of the procedures for preparing the intermediate products were found to be insufficiently detailed and consequently difficult to reproduce. The procedure described in the literature for the oxidation of perchloromethyl mercaptan [4] was especially inexact. In this procedure the nitric acid concentration and reaction temperature were not given when these data determine the conditions for the oxidation of perchloromethyl mercaptan and have a substantial effect on the yield of sulfonyl chloride. Thus, if perchloromethyl mercaptan was oxidized with nitric acid (d 1.52) complete destruction of the substance occurred and sulfonyl chloride was not obtained. By decreasing the amount and the concentration of nitric acid and increasing the time for heating the reaction mass, we were able to raise the yield of sulfonyl chloride considerably.

Trichloromethylcarbylamine chloride, it seemed, could be obtained by chlorination of trichloromethyl isothiocyanate. However, the isothiocyanate considered is unknown. In this work we tried to obtain trichloromethyl isothiocyanate by the isomerization of trichloromethyl thiocyanate. It is known that under certain conditions alkyl thiocyanates are capable of isomerizing into mustard oils [5-7]. In contrast to other thiocyanates, trichloromethyl thiocyanate could not be isomerized into trichloromethyl isothiocyanate. In all cases when the thiocyanate was heated in a sealed tube to 200° with CdI_2 or without CdI_2 and also when heated and irradiated with ultraviolet light without catalyst and with catalyst the starting material was recovered unchanged.

EXPERIMENTAL

Methylcarbylamine Chloride. With cooling by ice and salt, chlorine was passed into a solution of 41.3 g of methyl mustard oil in 50 ml of absolute ether at such a rate that the reaction temperature did not rise above 0-5°. After a brief passage of chlorine, a yellow precipitate formed and the amount of this increased at first. After 1 hour the color of the solution changed from yellow to red and the amount of precipitate decreased. Chlorination was complete after 2 hours 40 minutes, when a small amount of precipitate still remained. The reaction mixture was distilled. We obtained 54.3 g of substance. The yield was 85.7%.

B.p. 77.5-78°, d_4^{23} 1.2670, $n^{18}D$ 1.4487.

Found %: C 21.55; H 2.79; N 12.63; Cl 63.06; Cl_{act} 59.2. $C_2H_3NCl_2$. Calculated %: C 21.23; H 2.68; N 12.50; Cl 63.39; Cl_{act} 63.39.

When methyl isothiocyanate was chlorinated in ethyl chloride or chloroform and also without solvent, we were unable to isolate methylcarbylamine chloride in an individual state. Together with sulfur chlorides and carbylamine chloride, contaminated by various impurities, distillation of the reaction products yielded a large amount of hygroscopic and unstable needlelike crystals, which were probably the hydrochloride of carbylamine chloride. These crystals were not examined more closely.

Methylcarbylamine chloride was a colorless liquid with a sharp, irritating odor, and it reacted vigorously with alkalis and alcohols, was hydrolyzed by water and attacked rubber; guanidine derivatives were formed with amines.

A solution of 14.2 g of aniline in 30 ml of chloroform was added with ice-water cooling to 5.7 g of methylcarbylamine chloride, dissolved in 40 ml of dry chloroform and the reaction mass left to stand for some time at room temperature. After removal of the precipitate, the chloroform was distilled from the filtrate and then the residue kept in vacuum. In the flask remained a thick red mass, which was treated with alkali and ether. The ether extract was dried with solid alkali, the ether removed and the residue vacuum distilled. We isolated a substance with b.p. 153-155° (7 mm), which had a strongly alkaline reaction and was apparently diphenylmethylguanidine. The substance was not examined more closely.

Trichloromethylsulfonyl Chloride. 120-130 ml of nitric acid (d 1.4) was added with vigorous stirring over a period of 2.5 hours to a solution of 100 g of perchloromethyl mercaptan in 300 ml of glacial acetic acid,

first heated to 60-70°, and the reaction mixture was kept at this temperature. After the nitric acid had been added, the reaction mixture was heated on a boiling water bath until the evolution of nitrogen oxides ceased (2-2.5 hours), cooled and poured into an equal volume of cold water. The trichloromethylsulfonyl chloride precipitated was collected, washed well with water and dried over sulfuric acid or P_2O_5 in a vacuum desiccator. The yield was 70 g.

Reaction of Trichloromethylcarbylamine Chloride With Aniline. A solution of 3 g of aniline in 20 ml of ether was added dropwise to a solution of 0.7 g of trichloromethylcarbylamine chloride in 10 ml of absolute ether with cooling in ice water and the reaction mixture left to stand at room temperature for 3 hours. The precipitate was collected and washed carefully first with ether, then water to remove aniline hydrochloride, with soda solution and again with water to a neutral reaction to phenolphthalein. The water-insoluble residue was dried over phosphorus pentoxide in a vacuum desiccator. The product melted at 154-156°. The substance was recrystallized by solution in a small amount of chloroform and precipitation with ether. After two recrystallizations, the substance had m.p. 197-198°.

Found %: C 70.10; H 5.47; N 15.76; Cl 8.07. $C_{26}H_{24}N_5Cl$. Calculated %: C 70.67; H 5.44; N 15.85; Cl 8.05.

Di-(phenylamino)-chloromethyldiphenylguanidine was a white crystalline substance, which dissolved readily in chloroform, ethyl alcohol and acetonitrile but was insoluble in ether, ligroin and water.

After isolation of the di-(phenylamino)-chloromethyldiphenylguanidine, the ether – chloroform solution was evaporated and the residue recrystallized from alcohol. Two recrystallizations from 96% alcohol yielded a substance with m.p. 129-130°.

Found %: C 77.36; H 6.00; N 16.47. $C_{32}H_{30}N_6$. Calculated %: C 77.11; H 6.02; N 16.87.

Tri-(phenylamino)-methyldiphenylguanidine was a white crystalline substance, which dissolved readily in chloroform, ether, benzene and hot alcohol, with difficulty in cold alcohol and was insoluble in water.

Trichloromethyl Thiocyanate. With vigorous stirring and heating on a water bath, 20 g of powdered potassium cyanide was added in small portions to a solution of 18.5 g of perchloromethyl mercaptan in 40 ml of ether, preliminarily washed with water. When the potassium cyanide had been added, the reaction mixture was heated with stirring for a further 5 hours and was left overnight. The precipitate was then collected and washed with a small amount of ether. The filtrate was washed with water until the reaction for chlorine ion was negative. The ether layer was separated and dried with fired sodium sulfate. After removal of the ether, fractionation of the residue yielded trichloromethyl thiocyanate. The b.p. was 80° (49 mm). The yield was 48%. Trichloromethyl thiocyanate was obtained in the same yield if the reaction was carried out in ether with the addition of a small amount of water (about 0.5 g) during the reaction. A decrease in the amount of potassium cyanide led to a fall in the thiocyanate yield. The thiocyanate was formed in low yield by the method described in the literature [8].

SUMMARY

1. Previously undescribed methylcarbylamine chloride was obtained by chlorination of methyl isothiocyanate.

2. It was established that methyl- and trichloromethylcarbylamine chlorides did not react with hydrogen sulfide or sodium or copper sulfides. Methylcarbylamine chloride liberated iodine quantitatively from acidified solutions of potassium iodide. The action of aniline on trichloromethylcarbylamine chloride produced complete replacement of the chlorine atoms by the amine residue.

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CARBYLAMINE HALIDES

II. SYNTHESIS OF SECONDARY AMINES WITH A TRIFLUOROMETHYL GROUP

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Until now the only representative of secondary amines with a trifluoromethyl group at the nitrogen was hexafluorodimethylamine, which was obtained for the first time in low yield by fluorination of cyanogen iodide using IF_5 [1] and then by the addition of hydrogen fluoride to trifluoromethylcarbylamine fluoride by heating the reagents to 150° for 15 hours [2]. In contrast to the first, the second method of synthesis is recommended as a general procedure for preparing secondary amines with a trifluoromethyl group. However, due to the low accessibility of carbylamine fluorides, it also has very limited possibilities. Carbylamine fluorides are usually obtained by thermal decomposition of tri-(perfluoroalkyl)-amines [3]. Naturally, by the addition of hydrogen fluoride the perfluorocarbylamine fluorides thus formed can only be converted into secondary amines with perfluorinated radicals.

In this work a new method was developed for the preparation of secondary amines with a trifluoromethyl group, based on the interaction of hydrogen fluorides with carbylamine chlorides. As a result of the successive addition of hydrogen fluoride to carbylamine halides and the elimination of hydrogen chloride from the substances formed, secondary amines with a trifluoromethyl group were finally obtained.

$$R{-}N{=}CCl_2 \xrightarrow{+HF} RNHCCl_2F \xrightarrow{-HCl} RN{=}C\begin{matrix}Cl\\F\end{matrix} \xrightarrow{+HF}$$

$$\longrightarrow RNHCClF_2 \xrightarrow{-HCl} RN{=}CF_2 \xrightarrow{+HF} RNHCF_3$$

The addition of hydrogen fluoride at an N – C bond was also observed in other cases. Thus, hydrogen fluoride in ether solution readily adds to isocyanates in the cold, i.e., at room temperature with a quantitative formation of acid fluorides of carbamic acid [4].

The reaction of carbylamine chlorides with hydrogen fluoride proceeded vigorously in the cold and, depending on the reaction conditions, formed secondary amines or polymers of carbylamine fluorides. Thus, a reaction in ether with excess hydrogen fluoride formed alkyltrifluoromethylamines and in ethyl chloride or without solvent, the main reaction product was polymers of carbylamine fluorides. Evidently hydrogen fluoride produces polymerization of a carbylamine fluoride. It was not possible to isolate the intermediate carbylamine fluoride when the reaction was carried out in dilute solutions and with the calculated amount of hydrogen fluoride. In the latter case the original carbylamine chloride and the alkyltrifluoromethylamine were isolated.

The reaction was studied on the example of the interaction of hydrogen fluoride with phenyl-, p-tolyl-, β-chloroethyl- and trichloromethylcarbylamine chlorides; this yielded phenyltrifluoromethylamine (68.5%), p-tolyltrifluoromethylamine (70%), hexafluorodimethylamine (85%) and the acid fluoride of β-chloroethylcarbamic acid.

In the action of aniline on phenyltrifluoromethylamine, only 1 fluorine atom in the latter was replaced by an aniline residue and diphenylurea was only formed on treatment of the reaction product with water.

$$C_6H_5NHCF_3 + 2C_6H_5NH_2 \longrightarrow (C_6H_5NH)_2CF_2 + C_6H_5NH_2 \cdot HF$$
$$(C_6H_5NH)_2CF_2 + H_2O \longrightarrow (C_6H_5NH)_2CO + 2HF$$

Treatment of phenyltrifluoromethylamine with potassium fluoride with heating caused the elimination of hydrogen fluoride and the formation of phenylcarbylamine fluoride. This part of the investigation will be published in the next communication.

In contrast to the reaction of phenyl- and tolylcarbylamine chloride with hydrogen fluoride, in the preparation of hexafluorodimethylamine, if the reaction mixture was immediately heated to room temperature after the addition of the carbylamine chloride to hydrogen fluoride it was possible to isolate trichloromethylcarbylamine chloride and trichloromethylcarbylamine fluoride from the mixture together with hexafluorodimethylamine. The presence of trichloromethylcarbylamine fluoride in the reaction mixture serves as confirmation of the fact that the formation of amines proceeds through the formation of carbylamine fluorides, which evidently add hydrogen fluoride readily in the cold in contradiction to the data in [2].

The ease of hexafluorodimethylamine formation by the action of hydrogen fluoride on trichloromethylcarbylamine chloride may be explained by the successive addition of hydrogen fluoride to the carbylamine halides and the elimination of hydrogen chloride from the hexahalodimethylamines formed:

$$CCl_3N{=}CCl_2 \xrightarrow{+HF} CCl_3NHCCl_2F \xrightarrow{-HCl} CCl_3N{=}CClF \xrightarrow{+HF}$$
$$\longrightarrow CCl_3NHCClF_2 \xrightarrow{-HCl} CCl_3N{=}CF_2 \xrightarrow{+HF} CCl_3NHCF_3 \text{ etc.}$$

β-Chloroethylcarbylamine chloride also reacted vigorously with hydrogen fluoride in the cold. As in the case of phenylcarbylamine chloride, carrying out the reaction without solvent in excess hydrogen fluoride formed polymers of β-chloroethylcarbylamine fluoride. In only one of the experiments was it possible to isolate a small amount of a substance corresponding in fluorine and nitrogen content to β-chloroethyltrifluoromethylamine. When the reaction was carried out in diethyl or dimethyl ether, β-chloroethyltrifluoromethylamine could not be isolated. This was largely connected with the difficulty of separating the amine from oxonium salts of similar boiling points. If the reaction mixture was poured into a cold, saturated solution of potassium fluoride (in order to bind the excess hydrogen fluoride) and the organic layer quickly separated, fractional distillation of the latter yielded the acid fluoride of β-chloroethylcarbamic acid. Naturally, this acid fluoride could only have been formed as a result of hydrolysis of β-chloroethyltrifluoromethylamine.

$$ClCH_2CH_2NHCF_3 + H_2O \longrightarrow ClCH_2CH_2NHC\!\!<\!\!\begin{matrix}O\\F\end{matrix} + 2HF$$

The action of aniline on the acid fluoride yielded phenyl-β-chloroethylurea.

Evidently, in the hydrolysis of other amines with a trifluoromethyl group, acid fluorides of alkylcarbamic acids were also formed at first and not alkylcarbylamine fluorides as stated in [2]. The hydrolysis of hexafluorodimethylamine, proceeding to CO_2, F^- and NH_4^+ in an acid medium, may be represented by the following scheme:

$$CF_3NHCF_3 \xrightarrow{H_2O} CF_3NHC\!\!<\!\!\begin{matrix}O\\F\end{matrix} \xrightarrow{OH^-} CF_3NHC\!\!<\!\!\begin{matrix}O\\OH\end{matrix} \xrightarrow{-CO_2} CF_3NH_2 \xrightarrow{-HF}$$
$$\longrightarrow CF_2{=}NH \xrightarrow{-HF} FCN \xrightarrow{OH^-} HOCN$$
$$\downarrow OH^- \qquad\qquad \updownarrow$$
$$HNCO \qquad\qquad HNCO$$
$$HNCO + H_2O + H^+ \longrightarrow CO_2 + NH_4^+$$

The ideas of Haszeldine on the possibility of trifluoromethylcarbylamine fluoride formation under the conditions of secondary amine hydrolysis are unsubstantiated and therefore, as will be described in detail in the next communication, the dehydrofluorination of amines with a trifluoromethyl group proceeds only at high tem-

perature in the presence of potassium fluoride. The formation of the same hydrolysis products from hexafluorodimethylamine and trifluoromethylcarbylamine fluoride is evidently explained by the fact that the first stage in the hydrolysis of the carbylamine fluoride is the addition of water at the N=C bond and the formation of an unstable product, which is then decomposed to the acid fluoride of trifluoromethylcarbamic acid and then to CO_2, HF and NH_4^+.

EXPERIMENTAL

Phenyltrifluoromethylamine. a) Into a copper Wurtz flask, protected with a tube filled with fired magnesium sulfate and a Tishchenko bottle with sulfuric acid, was condensed 14.6 g of anhydrous hydrogen fluoride, 50 ml of absolute ether added and then 25 g of phenylcarbylamine chloride (5 moles of HF to 1 mole of carbylamine chloride) was introduced dropwise with cooling to -15 to -18°. The temperature of the reaction mixture was gradually raised to that of the room. Intense evolution of hydrogen chloride was observed at temperature above 0°. At the end of the evolution of hydrogen chloride, the ether and excess hydrogen fluoride were distilled from the reaction mixture at a pressure of 140-150 mm. The residue in the flask (35 g) was treated with potassium fluoride and, after removal of the precipitate, fractionated in vacuum. Two distillations yielded 16 g (68.5%) of product.

B.p. 50-51° (10 mm), d_4^{20} 1.2423, $n^{20}D$ 1.4652.

Found %: C 52.41; H 3.87; N 8.74; F 35.34. $C_7H_6NF_3$. Calculated %: C 52.20; H 3.71; N 8.70; F 35.40.

The colorless, clear liquid with a sharp odor was soluble in most organic solvents, but insoluble in water and slowly hydrolyzed by it. In aqueous acetone solution immediately after solution of the sample of substance at 0°, 0.35% of the fluorine was titratable, after 1.5 hours 9.63% and after 16 hours 36.01%. The product distilled readily in vacuum without attacking glass. At atmospheric pressure it boiled at 150-155° (with decomp.). It was unstable during storage, but was stabilized by the addition of a small amount of quinoline. It caused irritation of the mucous membranes of the eye. When heated with potassium fluoride it was converted into phenylcarbylamine fluoride; on treatment with aniline it formed diphenylurea.

To 0.8 g (1 mole)* of phenyltrifluoromethylamine was added 3.2 g (6 mole)* of aniline with water cooling and the mixture was heated on a water bath at 60° for 20 minutes. The pasty mass was treated with water and the excess aniline removed by the addition of dilute hydrochloric acid. The precipitate was collected, washed with water and dried. We obtained 0.7 g of a substance, which, after recrystallization from alcohol, melted at 235° and was found to be symmetrical diphenylurea. A mixed melting point of the substance with diphenylurea obtained from phosgene and aniline was not depressed.

b) To 5.8 g (2 mole)* of hydrogen fluoride was added 32 ml of absolute ether and 25.2 g (1 mole)* of phenylcarbylamine chloride and the reaction mixture left to stand for 4 hours at room temperature. After removal of the ether and hydrogen fluoride under the conditions described above, the residue was vacuum distilled to give 11.2 g of phenylcarbylamine chloride and 7.6 g of phenyltrifluoromethylamine.

B.p. 52° (12 mm), $n^{22}D$ 1.4610.

Found %: F 34.15. $C_7H_6NF_3$. Calculated %: F 35.4.

c) Into a copper flask was condensed 20 g of hydrogen fluoride, 60 g of ethyl chloride was added and then 35 g of phenylcarbylamine chloride was introduced over a period of 40 minutes with periodic stirring, when intense evolution of hydrogen chloride occurred and continued for 1.5 hours. During this time the temperature of the cooled mixture was kept at from 15 to 17° and then it was slowly raised to room temperature. After removal of the solvent and excess HF, the reaction mixture weighed 28 g. To the mixture was added 20 g of ethyl chloride and 10 g of fired potassium fluoride and the mixture left over night. On the following day the liquid was decanted from the precipitate and after evaporation of the ethyl chloride, the residue was vacuum distilled to give two fractions: 1st b.p. 63° (20 mm), 3.8 g. 2nd b.p. 127.5-130° (3 mm), 8.5 g.

The first fraction was found to be phenyltrifluoromethylamine.

B.p. 50-51° (10 mm), $n^{19}D$ 1.4649.

Found %: F 35.69. $C_7H_6NF_3$. Calculated %: F 35.4.

* As in original – Publisher's note.

A second distillation of the second fraction yielded the dimer of phenylcarbylamine fluoride.

B.p. 128-129° (2.5 mm) or 123-124° (1.6 mm), $n^{22}D$ 1.5208, d_4^{22} 1.2852.

Found %: N 10.11; F 27.32. M 263.6. $C_{14}H_{10}N_2F_4$. Calculated %: N 9.92; F 26.93. M 282.

The oily, colorless liquid was readily soluble in organic solvents but insoluble in water; it was hydrolyzed with difficulty by water and even by dilute solutions of alkalis.

Trifluoromethyl-p-toluidine was obtained analogously to phenyltrifluoromethylamine.

M.p. 38-40°, b.p. 66° (10 mm) or 75° (24 mm).

Found %: N 8.28; F 32.42. $C_8H_8NF_3$. Calculated %: N 8.00; F 32.57.

The product formed colorless, scaley crystals. It was readily soluble in organic solvents and insoluble in water; it was slowly hydrolyzed in aqueous acetone solutions; 5 minutes after solution of the sample of material, 5% of the fluorine could be titrated, after 30 minutes 12.4% and after 1.5 hours 26.2%. In the pure state it could be stored quite readily in a glass vessel.

Acid Fluoride of β-Chloroethylcarbamic Acid. a) Into a copper flask cooled to -15°, was condensed 7.4 g of hydrogen fluoride, and 30 ml of absolute ether and 15 g of β-chloroethylcarbylamine chloride were added. The reaction mixture was left at room temperature for 3.5 hours and then poured into a sufficient amount of a cold, saturated solution of potassium fluoride to bind the whole of the hydrogen fluoride used in the reaction. The ether layer was rapidly separated, the aqueous solution extracted 2-3 times with ether and the extract added to the main ether solution. The ether solution was dried with fired magnesium sulfate. After removal of the ether, the residue was fractionated in vacuum. We isolated 4.7 g of product.

B.p. 78-80° (6 mm), $n^{26}D$ 1.4350.

Found %: F 15.39; Cl 29.28. C_3H_5ONFCl. Calculated %: F 15.14; Cl 29.29.

The action of aniline on the acid fluoride yielded β-chloroethylphenylurea.

M.p. 117-118° (from 50% alcohol). Literature data: m.p. 124° [5].

Found %: N 13.76. $C_9H_{11}ON_2Cl$. Calculated %: N 14.11.

b) Dry hydrogen fluoride was slowly condensed into a copper tube cooled to -10 to -15° containing 18 g of β-chloroethylcarbylamine chloride, and hydrogen chloride was immediately liberated. After the condensation of hydrogen fluoride, the gain in weight of the reaction mixture was 8 g. The mixture was left for 12-14 hours while the temperature slowly rose to that of the room. The hydrogen fluoride and chloride were removed at a pressure of 150-200 mm at room temperature. To the residue in the flask (16.5 g) was added 5 g of fired potassium fluoride and the vacuum distillation continued. At 15 mm and room temperature 1.5 g of trifluoromethyl-β-chloroethylamine distilled and was condensed in a glass trap, cooled to -70°. The substance did not attack glass.

B.p. 76-77° (151 mm), d_4^{22} 1.4384, $n^{20}D$ 1.3670.

Found %: F 40.39; N 9.96. $C_3H_5NF_3Cl$. Calculated %: F 38.64; N 9.49.

The residue in the flask was extracted with ether and after removal of the solvent, it was vacuum distilled to give two fractions: 1st b.p. 65-68° (5 mm), 3.6 g; 2nd b.p. 83-112° (5 mm), 3 g.

A second distillation of the first fraction yielded β-chloroethylcarbylamine fluoride and apparently its dimer or trimer.

B.p. 81-82° (10 mm), d_4^{19} 1.4168, $n^{19}D$ 1.4162.

Found %: N 10.52; F 30.0; Cl 27.24. $(C_3H_4NF_2Cl)_n$. Calculated %: N 10.98; F 29.8; Cl 27.84.

The second fraction yielded what was probably a polymer of β-chloroethylcarbylamine fluoride with b.p. 122-123° (14 mm) and m.p. 47-48°.

Found %: N 11.09; F 25.18; Cl 28.01. $(C_3H_4NF_2Cl)_n$. Calculated %: N 10.98; F 29.8; Cl 27.84.

A low-boiling fraction with b.p. 76-77° (151 mm) was isolated in one experiment, but in the rest of the experiments only the last two fractions were isolated.

Hexafluorodimethylamine. Into a copper Wurtz flask was condensed 30 g of anhydrous hydrogen fluoride and 19 g of trichloromethylcarbylamine chloride (3 to 4-fold excess of HF) was added dropwise with cooling to -15°. The temperature of the reaction flask was kept at from -10 to -15° for 2 hours, raised to room temperature over a period of 1 hour and then the mixture heated at 30-35° for 30 minutes. The end of the reaction was determined by the cessation of hydrogen chloride evolution. In a copper receiver, cooled to -70°, condensed 13.2 g of a substance which was redistilled into a copper tube and then distilled on a Podbielniak column. We obtained 10 g of hexafluorodimethylamine. The b.p. was -6°.

Found %: C 15.72; H 0.83. M 153.1. C_2HNF_6. Calculated %: C 15.69; H 0.65. M 153.

SUMMARY

A method was developed for preparing secondary amines with a trifluoromethyl group at the nitrogen by the action of anhydrous hydrogen fluoride on carbylamine chlorides.

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AROMATIC HYDROCARBONS

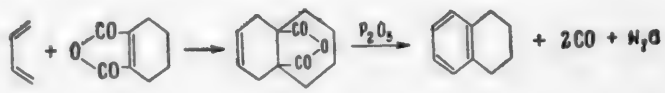
IX. SYNTHESIS OF HYDROCARBONS OF THE INDAN SERIES

V. R. Skvarchenko, L. A. Chervoneva, I. S. Pastukhova

and R. Ya. Levina

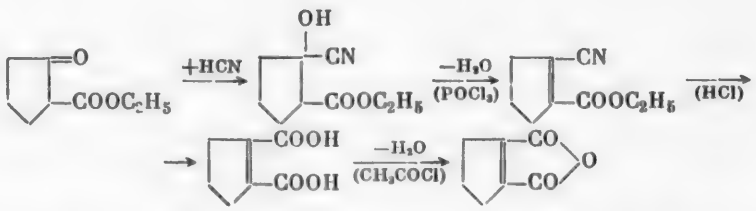
Moscow State University

Our previous discovery of the aromatization by phosphorus pentoxide of the adducts of conjugated diene hydrocarbons with maleic and alkylmaleic anhydrides [1-5] was used in previous work [6] for the synthesis of hydrocarbons of the tetralin series; in this case the dienophile used was a cyclic analog of maleic anhydride, the anhydride of Δ1-cyclohexenedicarboxylic-1,2 acid:

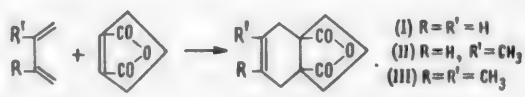


In order to prepare hydrocarbons of the indan series, in the present work we used phosphorus pentoxide to aromatize adducts of diene hydrocarbons with another cyclic analog of maleic anhydride, the anhydride of Δ1-cyclopentenedicarboxylic-1,2 acid.

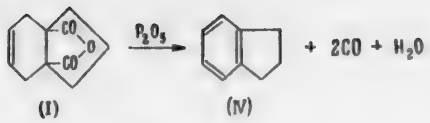
This dienophile was obtained from the ethyl ester of cyclopentanone-2-carboxylic acid [7] by the following scheme [8-10]:



By reacting the anhydride of Δ1-cyclopentenedicarboxylic-1,2 acid with the alkadienes divinyl, isoprene and 2,3-dimethylbutadiene-1,3 by prolonged heating in an autoclave, we obtained the previously undescribed adducts, the anhydride of 4,7,8,9-tetrahydroindandicarboxylic-8,9 acid (I) and its homologs, the anhydrides of 5-methyl- and 5,6-dimethyl-4,7,8,9-tetrahydroindandicarboxylic-8,9 acids (II) and (III).

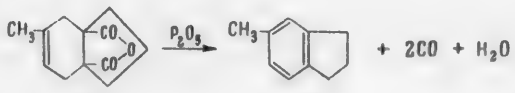


The interaction of the anhydride of 4,7,8,9-tetrahydroindandicarboxylic-8,9 acid (I) with phosphorus pentoxide gave indan (IV) (69% yield):



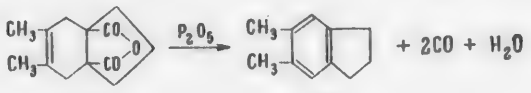
(I) (IV)

Heating the anhydride of 5-methyl-4,7,8,9-tetrahydroindandicarboxylic-8,9 acid (II) with phosphorus pentoxide yielded 5-methylindan [(V), 61% yield].



(II) (V)

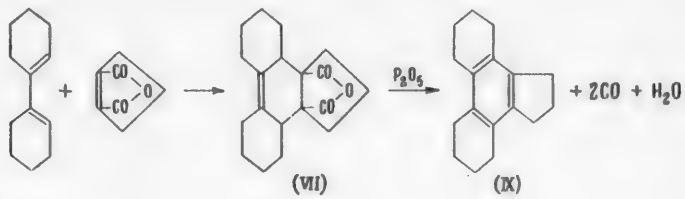
5,6-Dimethylindan [(VI), 84% yield] was obtained by the interaction of phosphorus pentoxide with the anhydride of 5,6-dimethyl-4,7,8,9-tetrahydroindandicarboxylic-8,9 acid (III).



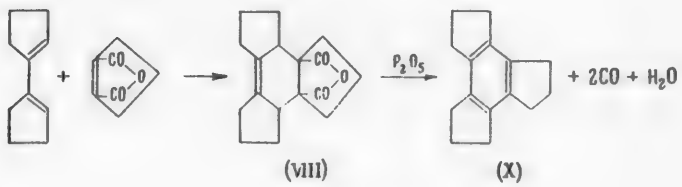
(III) (VI)

The hydrocarbons obtained were identified from their constants and the melting points of their sulfonamides.

From the anhydride of Δ1-cyclopentenedicarboxylic-1,2 acid we also obtained adducts with bicyclic diene hydrocarbons (1,1'-dicyclohexenyl and 1,1'-dicyclopentenyl) and these were the anhydrides of 4,5,6,7-dicyclohexano- and 4,5,6,7-dicyclopentano-4,7,8,9-tetrahydroindandicarboxylic-8,9 acids (VII) and (VIII); by reaction with phosphorus pentoxide, these adducts were converted into the polynuclear aromatic hydrocarbons 4,5,6,7-dicyclohexanoindan [(IX), 44% yield, characterized by conversion into dibenzoindan by heating with selenium] and 4,5,6,7-dicyclopentanoindan [(X), 58% yield], respectively:



(VII) (IX)



(VIII) (X)

EXPERIMENTAL

Adducts of Diene Hydrocarbons With the Anhydride of Δ1-Cyclopentenedicarboxylic-1,2 Acid

Adduct of Divinyl (I). The anhydride of Δ1-cyclopentenedicarboxylic-1,2 acid [10 g, 0.07 mole, b.p. 133-135° (10 mm), $n^{20}D$ 1.4978; literature data [10]: b.p. 130° (5 mm)] and divinyl (20 ml, 0.21 mole) were heated in an autoclave at 150° for 23 hours in the presence of a small amount of hydroquinone. Recrystallization of the reaction mass from ligroin yielded the anhydride of 4,7,8,9-tetrahydroindandicarboxylic-8,9 acid (12 g, 92%) with m.p. 114-115° (not described in the literature).

Found %: C 68.81, 68.91; H 6.50, 6.53. $C_{11}H_{12}O_3$. Calculated %: C 68.73; H 6.30.

Adduct of Isoprene (II) was obtained under the same conditions. From 11.8 g (0.08 mole) of the anhydride Δ1-cyclopentenedicarboxylic-1,2 acid and 20.3 ml (0.2 mole) of isoprene we obtained 12.6 g (76%) of the anhydride of 5-methyl-4,7,8,9-tetrahydroindandicarboxylic-8,9 acid (not described in the literature) with m.p. 40-41° (from ligroin).

Found %: C 70.17, 70.13; H 7.12, 7.08. $C_{12}H_{14}O_3$. Calculated %: C 69.89; H 6.84.

Adduct of 2,3-Dimethylbutadiene-1,3 (III). A mixture of the anhydride of Δ1-cyclopentenedicarboxylic-1,2 acid (9.1 g, 0.06 mole), dimethylbutadiene (11 g, 0.12 mole) and hydroquinone (0.1 g) was heated for 20 hours in an autoclave at 110°. The thick oil obtained partially crystallized on cooling; recrystallization of the precipitated crystals from ligroin yielded the anhydride of 5,6-dimethyl-4,7,8,9-tetrahydroindandicarboxylic-8,9 acid (11 g, 78%, not described in the literature) with m.p. 61.5-62.5°.

Found %: C 71.06, 71.06; H 7.47, 7.49. $C_{13}H_{16}O_3$. Calculated %: C 70.88; H 7.32.

Adduct of 1,1'-Dicyclohexenyl (VII) was obtained by heating the anhydride of Δ1-cyclopentenedicarboxylic-1,2 acid (4.5 g, 0.03 mole) with 1,1'-dicyclohexenyl (4 g, 0.03 mole) and hydroquinone (0.1 g) in 5 ml of xylene on an oil bath at 150° for 9 hours. The anhydride of 4,5,6,7-dicyclohexano-4,7,8,9-tetrahydroindandicarboxylic-8,9 acid (5.7 g, 67%), obtained after removal of the xylene, melted at 138-139° (from alcohol). Literature data [11]: m.p. 140°.

Adduct of 1,1'-Dicyclopentenyl (VIII) was obtained by the procedure described above for the adduct of 1,1'-dicyclohexenyl. From 3.5 g (0.025 mole) of the anhydride of Δ1-cyclopentenedicarboxylic-1,2 acid and 3.5 g (0.025 mole) of 1,1'-dicyclopentenyl we obtained the anhydride of 4,5,6,7-dicyclopentano-4,7,8,9-tetrahydroindandicarboxylic-8,9 acid (3.6 g, 52%) with m.p. 89-89.5° (from alcohol). Literature data [11]: m.p. 90°.

Preparation of Hydrocarbons of the Indan Series

Indan (IV). The anhydride of 4,7,8,9-tetrahydroindandicarboxylic-8,9 acid [(I), 7.5 g, 0.04 mole] was heated with phosphorus pentoxide (5.5 g, 0.04 mole) on a metal bath from 100 to 280°. When the evolution of carbon monoxide ceased, the reaction product was vacuum distilled, dissolved in ligroin and heated for 1 hour with a 20% solution of sodium hydroxide to remove possible traces of the original adduct. The solution was washed with water, dried with calcium chloride, the ligroin removed and the residue vacuum distilled to yield indan (3.2 g, 69%).

B.p. 65-66° (17 mm), $n^{20}D$ 1.5369, d_4^{20} 0.9591, MR_D 38.47. $C_9H_{10}F_3$. Calculated 37.96.

Sulfonamide: m.p. 131-132° (from dilute alcohol).

Literature data: b.p. 70-71° (18 mm), $n^{20}D$ 1.5367, d_4^{20} 0.963, MR_D 38.34 [12]; sulfonamide: m.p. 132-133° [13].

5-Methylindan (V). 5-Methyl-4,7,8,9-tetrahydroindandicarboxylic-8,9 acid [(IV), 5.2 g, 0.02 mole] was reacted with phosphorus pentoxide (3.0 g, 0.02 mole) under the same conditions as described above. The evolution of carbon monoxide ceased when the mixture was gradually heated from 100 to 320°. The 5-methylindan (2 g, 61%) obtained had the following constants:

B.p. 101-102° (32 mm), $n^{20}D$ 1.5308, d_4^{20} 0.9501, MR_D 43.03. $C_{10}H_{12}F_2$. Calculated 42.58.

Literature data [14]: b.p. 74° (11 mm), $n^{20}D$ 1.5332, d_4^{20} 0.9494, MR_D 43.17.

The sulfonamide of 5-methylindan (not described in the literature) melted at 155-156° (from dilute alcohol).

Found %: N 6.49, 6.44. $C_{10}H_{13}O_2NS$. Calculated %: N 6.62.

5,6-Dimethylindan (VI). When gradually heated from 120 to 320° with phosphorus pentoxide (6.0 g, 0.04 mole) under the conditions described above, the anhydride of 5,6-dimethyl-4,7,8,9-tetrahydroindandicarboxylic-8,9 acid [(III), 9.5 g, 0.04 mole] yielded 5,6-dimethylindan (5.3 g, 84%).

B.p. 93-95° (10 mm), $n^{20}D$ 1.5272, d_4^{20} 0.9449, MR_D 47.58. $C_{11}H_{14}F_2$. Calculated 47.20.

Found %: C 90.21, 90.30; H 9.94, 9.86. $C_{11}H_{14}$. Calculated %: C 90.34; H 9.66.

Sulfonamide of 5,6-dimethylindan – m.p. 175-176° (from dilute alcohol).

Found %: N 5.95, 6.14. $C_{11}H_{15}O_2NS$. Calculated %: N 6.20.

Literature data [17]: b.p. 115° (25 mm), $n^{26.5}D$ 1.5314.

4,5,6,7-Dicyclohexanoindan (IX). A mixture of the anhydride of 4,5,6,7-dicyclohexano-4,7,8,9-tetrahydroindandicarboxylic-8,9 acid [(VII), 5.7 g, 0.02 mole] and phosphorus pentoxide (2.7 g, 0.02 mole) was heated on a metal bath at 120-290° until the evolution of carbon monoxide ceased. The reaction mass was extracted several times with boiling ligroin and removal of the solvent from the extracts and recrystallization of the residue from alcohol yielded 4,5,6,7-dicyclohexanoindan (1.8 g, 44%) with m.p. 152-153°.

Found %: C 90.05, 90.17; H 9.94, 9.93. $C_{17}H_{22}$. Calculated %: C 90.20, H 9.80.

Literature data [15]: m.p. 153°.

4,5,6,7-Dibenzoindan (obtained by heating dicyclohexanoindan with selenium for 7 hours at 300-320°) had m.p. 147-148 (from alcohol). The picrate of 4,5,6,7-dibenzoindan had m.p. 163-164° (from alcohol).

Literature data [11]; dibenzoindan m.p. 149°; its picrate m.p. 165-166°.

4,5,6,7-Dicyclopentanoindan [(X), Tricyclopentanobenzene]. A mixture of the anhydride of 4,5,6,7-dicyclopentano-4,7,8,9-tetrahydroindandicarboxylic-8,9 acid [(VIII), 3.6 g, 0.01 mole] and phosphorus pentoxide (1.9 g, 0.013 mole) was heated on a metal bath at 150-250° until the evolution of carbon monoxide ceased. The reaction mass was extracted with boiling ligroin. After removal of the solvent, the residue was recrystallized from methyl alcohol. The dicyclopentanoindan obtained (1.5 g, 58%) had m.p. 96-96.5° (from methyl alcohol). A mixed melting point with dicyclopentanoindan obtained by the condensation of cyclopentanone under the action of hydrogen chloride [16] was not depressed. Literature data [11]: m.p. 96-97°.

SUMMARY

1. A new preparative method was developed for the synthesis of hydrocarbons of the indan series by aromatization under the action of phosphorus pentoxide of the adducts of diene hydrocarbons with the anhydride of Δ1-cyclopentenedicarboxylic-1,2 acid. By this method we obtained indan (69% yield), 5-methylindan (61% yield), 5,6-dimethylindan (84% yield), 4,5,6,7-dicyclohexanoindan (44% yield) and 4,5,6,7-dicyclopentanoindan (58% yield).

2. We obtained for the first time the adducts of Δ1-cyclopentenedicarboxylic-1,2 acid with the alkanedienes divinyl (the anhydride of 4,7,8,9-tetrahydroindandicarboxylic-8,9 acid, 92% yield), isoprene (the anhydride of 5-methyl-4,7,8,9-tetrahydroindandicarboxylic-8,9 acid, 79% yield) and 2,3-dimethylbutadiene-1,3 (the anhydride of 5,6-dimethyl-4,7,8,9-tetrahydroindandicarboxylic-8,9 acid, 78% yield).

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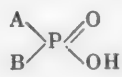
APPLICATION OF THE HAMMETT EQUATION TO THE IONIZATION CONSTANTS OF PHOSPHOROORGANIC ACIDS IN 7 AND 80% ALCOHOL

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One of us recently showed [1] that the Hammett equation [2] $\lg\frac{K}{K_0} = \rho\Sigma\sigma$ or in another form, $pK = pK_0 - \rho\Sigma\sigma$, could be applied to the ionization constants of phosphorus acids of the general type



where the P=O group plays the part of a conducting system similar to an aromatic ring in the usual application of the Hammett equation and A and B may be alkyl, aryl, alkoxyl or hydroxyl groups, hydrogen or the O^- ion. On a large number of phosphorus acids it was shown that for aqueous or 50% alcohol solution a linear dependence of pK on $\Sigma\sigma$ was maintained with good correlation coefficients (from 0.955 to 0.993). Taking hypophosphoric acid (A = B = H; $pK_0 = 1.00$; $\Sigma\sigma = 0$), as the standard, it was found possible to calculate the constants σ for 56 substituents, the constants ρ for the first and second stages of ionization of acids of this type in water (0.99 and 1.788) and in 50% alcohol (1.312 and 1.358) and the corresponding pK_0 values.

In connection with investigations in the field of tautomerism of phosphoroorganic compounds [3], we measured the apparent ionization constants of a series of phosphorus acids in 7 and 80% aqueous alcohol. It seemed interesting to check how well the Hammett equation was obeyed in these solvents. This was all the more interesting as we had determined the ionization constants of certain types of phosphorus acids which had not been measured previously, namely those of diarylphosphinic (A = B = Ar) and diarylphosphoric acids (A = B = = ArO). The results obtained are presented in Table 1 together with certain data, which we obtained previously [3] (marked with asterisks).

The constants σ for aroxy groups at phosphorus were unknown. To calculate them we determined the apparent ionization constants (pK_1 and pK_2) of phenyl- and diphenylphosphoric and also of tolyl- and ditolyphosphoric acids in 50% alcohol, since the ρ and pK_0 constants for the ionization of phosphorus acids in this solvent can be determined with high accuracy [1]. Results were obtained (Table 2) from which we calculated the average values of σ for C_6H_5O- and C_7H_7O- groups, presented in the last column of Table 2.

The values of σ found were used for constructing a graph of pK f($\Sigma\sigma$) in 7 and 80% alcohol and were made more precise by allowing for data obtained in these two solvents. The probable average values obtained finally were as follows: for the group C_6H_5O $\sigma = -0.061 \pm 0.012$ (n = 7); for the group $CH_3C_6H_4O$ $\sigma = -0.141 \pm 0.011$ (n = 8).

One of us deduced the constants σ for phenyl and p-tolyl groups at phosphorus from the data of Jaffe, Freedman and Doak [4], who determined the ionization constants of phenyl- and tolylphosphinic acids in water and 50% aqueous alcohol. The corresponding average values of σ were found for C_6H_5 (-0.481 ± 0.010). and for p-$CH_3C_6H_4$ groups (0.602 ± 0.010). However, it was found that the use of these σ constants for diphenylphosphinic

TABLE 1

Ionization Constants of Some Phosphorus Acids

No.	Formula	7% alcohol		80% alcohol	
		pK_1	pK_2	pK_1	pK_2
1	$(CH_3O)_2POOH$ *	1.25	—	3.01	—
2	$(C_2H_5O)_2POOH$ *	1.37	—	3.15	—
3	$(C_3H_7O)_2POOH$ *	1.52	—	3.29	—
4	$C_6H_5OPO(OH)_2$	1.46	6.29	3.36	8.71
5	$(C_6H_5O)_2POOH$	...	—	2.71	—
6	$p\text{-}CH_3C_6H_4OPO(OH)_2$	1.64	6.45	3.45	8.81
7	$(p\text{-}CH_3C_6H_4O)_2POOH$	1.36	—	2.91	—
8	$(CH_3)_2POOH$	3.13	—	5.15	—
9	$(C_4H_9)_2POOH$	3.50	—	5.63	—
10	$(iso\text{-}C_4H_9)_2POOH$	3.70	—	5.63	—
11	$(C_6H_5)_2POOH$	2.32	—	4.24	—
12	$(p\text{-}CH_3C_6H_4)_2POOH$	2.47	—	4.45	—
13	$(p\text{-}ClC_6H_4)_2POOH$	1.68	—	3.48	—
14	$(p\text{-}NO_2C_6H_4)_2POOH$	...	—	2.37	—

TABLE 2

Ionization Constants of Arylphosphoric Acids in 50% Alcohol

No.	Formula	pK	σ*	$\bar{\sigma}$ (average)
4	$C_6H_5OPO(OH)_2$	2.61	—0.064	—0.073
4	$C_6H_5OPO(O^-)OH$	7.66	—0.052	
5	$(C_6H_5O)_2POOH$	2.28	—0.103	
6	$p\text{-}CH_3C_6H_4OPO(OH)_2$	2.69	—0.125	—0.116
6	$p\text{-}CH_3C_6H_4OPO(O^-)OH$	7.74	—0.105	
7	$(p\text{-}CH_3C_6H_4O)_2POOH$	2.32	—0.118	

or, correspondingly, di-p-tolylphosphinic acids led to a sharp deviation of the points corresponding to these acids from the linear dependence $pK = pK_0 - \rho\Sigma\sigma$ in 7 and 80% alcohol, which was obeyed well for all the other acids.

To determine the reason for this deviation we measured the apparent ionization constants of diphenylphosphinic and di-p-tolylphosphinic acids in 50% alcohol. We obtained pK values equal to 3.43 and 3.66 and σ values for phenyl and p-tolyl groups of -0.542 and -0.629, respectively. At these values of σ, the points corresponding to diphenyl- and di-p-tolylphosphinic acids lay well on the line of $pK = pK_0 - \rho\Sigma\sigma$ in 7 and 80% alcohol. These values of σ were then made more precise by allowing for the data from measurements in 7 and 80% alcohol and finally the following average probable values were obtained: for C_6H_5 $\sigma = -0.592 \pm 0.017$ (n = 3); for $p\text{-}CH_3C_6H_4$ $\sigma = -0.674 \pm 0.016$ (n = 3). Thus the value of σ for phenyl or tolyl groups depends on the number of these groups at the phosphorus atom (for phenyl, -0.481 with one and -0.592 with two; for tolyl, -0.602 with one and -0.674 with two). Apparently this phenomenon is connected with the steric hindrance effect of two phenyl (tolyl) groups at one phosphorus atom. The figure shows graphs of $pK = pK_0 - \rho\Sigma\sigma$ in 7 (I) and 80% (II) alcohol, constructed from data in Table 1 using the constants σ deduced previously,* and the new values found in the present work for the groups C_6H_5O, $p\text{-}CH_3C_6H_4O$, C_6H_5 and $p\text{-}CH_3C_6H_4$.

The values of ρ, pK_0 and the correlation coefficients r, calculated by the method of least squares, are presented in Table 3.

*There were printing errors in the table of the constants σ in the publication [1]. We take this opportunity to correct them:

Group	Printed	Correct value
$iso\text{-}C_3H_7$	−0.300	−1.300
C_4H_9	−0.219	−1.219

TABLE 3

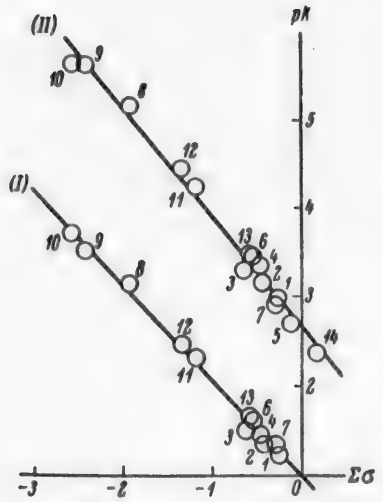
Values of ρ, pK_0 and r for the Ionization Constants of Phosphoroorganic Acids

Solvent (alcohol)	ρ	pK_0	r
7%	1.050	1.01	0.996
80%	1.219	2.68	0.994

TABLE 4

Characteristics of Phosphoroorganic Acids Investigated

Formula	Melting point	Neutralization equivalent		Melting point according to literature data
		found	calculated	
$C_6H_5OPO(OH)_2$	100 —101°	87.2, 87.3	87.1	100—101° [6]
$(C_6H_5O)_2POOH$	70 —71	250.7, 249.7	250.2	71 [7, 8]
$p\text{-}CH_3C_6H_4OPO(OH)_2$	114 —115	94.2, 94.2	94.1	116 [9]
$p\text{-}(CH_3C_6H_4O)_2POOH$ *	80.5— 81.5	277.8, 279.0	278.2	—
$(CH_3)_2POOH$	87 — 88.5	94.6, 94.4	94.1	87.5—88.5 [10]
$(C_4H_9)_2POOH$	70 — 71	178.4, 178.5	178.2	70.5—71 [11]
$(iso\text{-}C_4H_9)_2POOH$	43 — 45	177.9, 178.0	178.2	43—45 [12]
$(C_6H_5)_2POOH$	192	218.4, 218.4	218.2	190—192 [13]
$(p\text{-}CH_3C_6H_4)_2POOH$	132 —133	246.1, 246.0	246.2	131—132 [14]
$(p\text{-}ClC_6H_4)_2POOH$	133 —134	287.4, 287.3	287.0	133—135 [15]
$(m\text{-}NO_2C_6H_4)_2POOH$	270 —271	308.6, 308.6	308.2	268 [16, 17]



Application of the Hammett equation to the ionization constants of phosphoroorganic acids in 7 and 80% alcohol.

EXPERIMENTAL

The pK values were determined by measuring the pH of partially neutralized solutions (30, 50 and 70% neutralization), using a glass electrode and the tube potentiometers LP-5 and LP-51 with calibration according to a biphthalate buffer with pH 4.00. No correction was introduced for the change in activity in going from water to 80% alcohol. The concentration of the solutions measured was $5 \cdot 10^{-3}$ M (ionic strength of solution did not exceed 0.025). The temperature was 20°. The value of pK was calculated according to Kumler's formula [5] in which the term $\frac{K_W}{H^+}$ is neglected.

The distilled water was additionally purified by passage through two columns with anion and cation exchange resins (type MMG-1 and MSF). The alcohol was purified in the usual way. The acids investigated were synthesized and purified according to the methods described for them. Table 4 gives the melting points and neutralization equivalents of the acids used in comparison with literature data.

SUMMARY

1. From a determination of the ionization constants of a series of phosphorus acids in 7 and 80% alcohol it was established that in accordance with the Hammett equation the indices of the ionization constant bore a linear relationship to the constants σ, deduced previously and specific for phosphoroorganic compounds.

2. The constants σ were determined for C_6H_5O and p-$CH_3C_6H_4O$ groups at a phosphorus atom.

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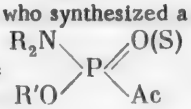
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ORGANOPHOSPHORUS INSECTICIDES

VI. AMIDOESTERS OF THIOPHOSPHORIC AND DITHIOPHOSPHORIC ACIDS CONTAINING THE β-ETHYLMERCAPTOETHYL GROUPING

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M. P. Shabanova, L. F. Efimova and N. M. Gamper
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The insecticide properties of amides of phosphoric and thiophosphoric acids were discovered in 1936 by G. Schrader [1], who synthesized a series of derivatives of dialkylamidophosphoric and dialkylamidothiophosphoric acids of the type  , where R and R' are alkyls and Ac is a substituent of an acyl character such as Cl, F, CN, CNO, CH_3COO etc. These compounds had a contact insecticide action. Tetraalkyldiamidofluorophosphates and octamethyltetraamidopyrophosphates were then prepared [1] and these compounds were insecticides with a strong systemic action. Subsequently a series of authors synthesized a large number of amidoesters of phosphoric and thiophosphoric acids, containing substituted phenyl [1, 2], azide [3] and other [4, 5] groups. In addition, a series of amides and amidoesters of pyrophosphoric acid were prepared [6, 7].

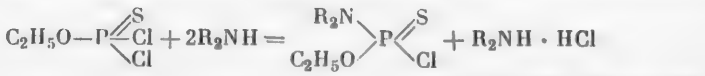
Most insecticides, amides of phosphorus acids, are characterized by a weak contact and a strong systemic action. Such systemic insecticides as tetramethyldiamidofluorophosphate (Dimefox [1]), diisopropyldiamidofluorophosphate (Isopestox [8]) and octamethyltetraamidopyrophosphate (Octamethyl [1]) have found practical application.

On the other hand, it is known that insecticides that are derivatives of thiophosphoric and dithiophosphoric acids, containing the β-alkylmercaptoethyl grouping, such as Mercaptophos [9] (a mixture of O,O-diethyl-O-β-ethylmercaptoethylthiophosphate and O,O-diethyl-S-β-ethylmercaptoethylthiophosphate), the preparation M-81 [10] (O,O-dimethyl-S-β-ethylmercaptoethyldithiophosphate) etc, also have a strong systemic action.

It seemed interesting to prepare and investigate the insecticide activity of amidoesters of thiophosphoric and dithiophosphoric acids, containing the β-ethylmercaptoethyl grouping. It was to be expected that compounds of this type would also have a strong systemic action.

Until now, amidoesters of thiophosphoric acid and dithiophosphoric acid containing a β-ethylmercaptoethyl grouping were unknown. There are only descriptions of some amidoesters of phosphoric acid containing β-methylmercaptoethyl [11] and β-ethylmercaptoethyl groupings [12]. There is no detailed information in the literature on the insecticide properties of these compounds.

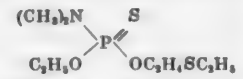
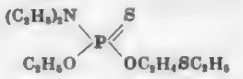
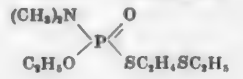
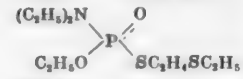
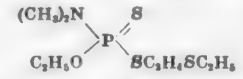
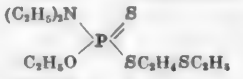
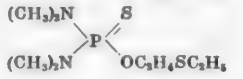
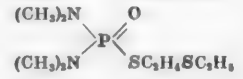
As starting materials for the synthesis of amidoesters of thiophosphoric and dithiophosphoric acids containing a β-ethylmercaptoethyl grouping we used ethyl dimethylamidochlorothionephosphate (I), ethyl diethylamidochlorothionephosphate (II) and tetramethyldiamidochlorothionephosphate (III). The first two acid chlorides were obtained by the action of dimethylamine or diethylamine on ethyl dichlorothionephosphate



(I) R = CH_3; (II) R = C_2H_5

TABLE 1

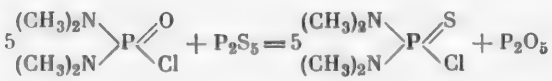
Constants and Yields of Insecticides Obtained

Laboratory number	Formula	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	MR_D found	MR_D calculated	Yield (in %)
Gd-50		112—114 (2.5)	1.5015	1.1091	68.52	68.93	49
Gd-52		118—120 (2)	1.4972	1.0779	77.54	78.17	24
Gd-53		122—123 (2.5)	1.5100	1.1272	68.28	68.64	64
Gd-54		142—143 (3)	1.5046	1.0884	77.51	77.54	61
Gd-55		136—137 (2.5)	1.5501	1.1409	76.36	76.31	42
Gd-56		133—134 (2)	1.5430	1.1113	85.60	85.64	32
Gd-64		105—106 (1.5)	1.5151	1.1008	70.25	70.23	50
Gd-66		103—104 (1)	1.5208	1.1165	69.90	69.93	72

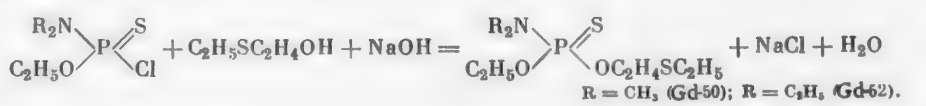
Tetramethyldiamidochlorothiophosphate was synthesized both by the reaction of dimethylamine with phosphorus thiotrichloride,

$$PSCl_3 + 4(CH_3)_2NH = \underset{(III)}{[(CH_3)_2N]_2PSCl} + 2(CH_3)_2NH \cdot HCl,$$

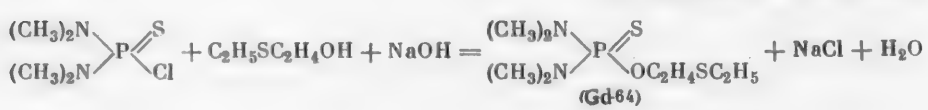
and by heating tetramethyldiamidochlorophosphate with phosphorus pentasulfide by a method analogous to that we developed for the preparation of acid chlorides of thiophosphinic acids [13]:



By the action of β-hydroxydiethyl sulfide on the acid chlorides described above in the presence of powdered sodium hydroxide we synthesized O-ethyl-O-β-ethylmercaptoethyldimethylamidothiophosphate (Gd-50), O-ethyl-O-β-ethylmercaptoethyldiethylamidothiophosphate (Gd-52) and O-β-ethylmercaptoethyltetramethyldiamidothiophosphate (Gd-64).



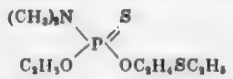
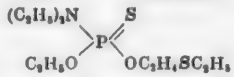
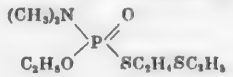
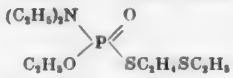
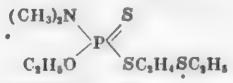
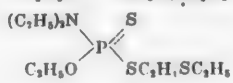
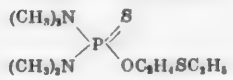
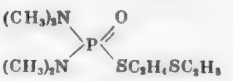
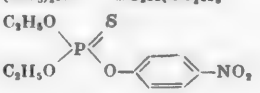
R = CH_3 (Gd-50); R = C_2H_5 (Gd-52).



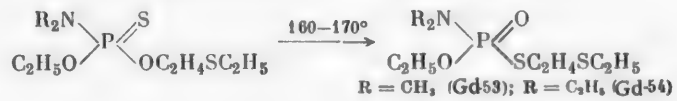
(Gd-64)

TABLE 2

Comparative Toxicity of Compounds for Muchnistyi Chervets and Bugs of Vrednii Cherepashki by Contact Action

Laboratory number	Formula	Muchnistyi chervets	Vrednii cherepashki
		LD_{85-100}* dead, paralyzed in 7 days	mort. autumn bugs from emuls. 0.005% conc. in 7 days
Gd-50		> 0.5	0
Gd-52		0.5	—
Gd-53		> 0.5	25.0
Gd-54		0.5	27.5
Gd-55		0.3	45.0
Gd-56		0.3	90.0
Gd-64		0.5	—
Gd-66		< 0.5	—
Thiophos		0.03	100*

When heated at 160-170° for 8-10 hours, the compounds obtained were isomerized into O-ethyl-S-β-ethylmercaptoethyldimethylamidothiophosphate (Gd-53), O-ethyl-S-β-ethylmercaptoethyldiethylamidothiophosphate (Gd-54) and S-β-ethylmercaptoethyltetramethyldiamidothiophosphate (Gd-66), respectively.

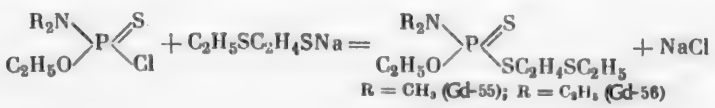


R = CH_3 (Gd-53); R = C_2H_5 (Gd-54)



(Gd-66)

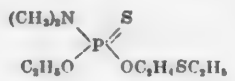
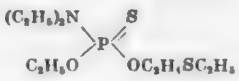
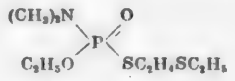
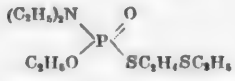
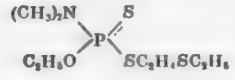
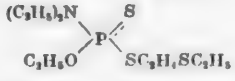
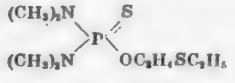
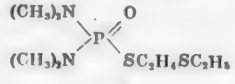
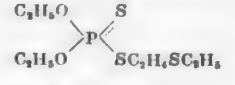
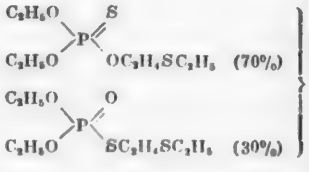
In addition, by the reaction of ethyl dimethylamidochlorothionephosphate and ethyl diethylamidochlorothionephosphate with the sodium derivative of β-mercaptodiethyl sulfide we obtained O-ethyl-S-β-ethylmercaptoethyldimethylamidodithiophosphate (Gd-55) and O-ethyl-S-β-ethylmercaptoethyldiethylamidodithiophosphate (Gd-56).



R = CH_3 (Gd-55); R = C_2H_5 (Gd-56)

TABLE 3

Comparative Evaluation of Systemic Action of Compounds Against Arachnoid Mites and Bugs of Vrednii Cherepashki (emulsion concentration 0.05)

Laboratory number	Formula	Arachnoid mites: fall in number of mites as % orig. number with control correction					Vrednii cherepashki
		1	5	10	15	20	% mort. autumn bugs fed on wheat wetted with 0.6% emuls.
Gd-50		0	0	0	0	0	0
Gd-52		30.1	26.1	19.6	18.1	10.5	—
Gd-53		66.0	79.2	88.6	83.6	66.3	12.5
Gd-54		66.5	89.3	97.7	95.9	90.7	12.5
Gd-55		33.3	46.6	51.1	46.2	—	37.5
Gd-56		64.4	91.3	99.1	95.3	90.2	30.0
Gd-64		4.0	22.7	18.6	0	—	10.0
Gd-66		4.6	17.5	22.7	10.1	—	5.0
Gd-74		—	—	—	—	—	97.5
Mercaptophos	Mixture of isomers:  (70%) (30%)	76.3	93.2	98.0	96.8	96.5	

The constants and yields of the new insecticides obtained are presented in Table 1.

The compounds synthesized were studied in laboratory experiments as contact and systemic insecticides and acaricides. They were used in the form of emulsions, prepared from 30% concentrates containing 30% of the active substance and 70% of the auxiliary substance OP-7. In all experiments the concentrations of the working emulsions are given as the active principle.

As previously [10], the contact action of the compounds was investigated on the larvaeof muchnistyi chervets (Pseudococcus maritimus Ehrh.) at an advanced stage by spraying the insects and on autumn bugs of vrednii cherepashki (Eurygaster integriceps Put.) by immersing them in the emulsion for 5 seconds. A comparative evaluation of the toxicity of the compounds was carried out for muchnistyi chervets through concentrations producing 95-100% dead and paralyzed insects (LD_{95-100}) on the seventh day and for bugs of vrednii cherepashki through the mortality of the insects (in %) from an emulsion of 0.005% concentration on the fifth day. The data of the experiments are shown in Table 2, which shows that the amidoesters of thiophosphoric and dithiophosphoric acids tested were weak contact insecticides for muchnistyi chervets for which LD_{95-100} equalled 0.3-0.5%, while Thiophos gives the same effect at a concentration of 0.03%.

The compound Gd-56 was found to be quite active against the bugs of vrednii cherepashki and at a concentration of 0.005% it produced 90% mortality of the insects, while Thiophos at a concentration of 0.0025% produced 97.5% mortality.

The same table shows that the derivatives of dithiophosphoric acid (Gd-55 and Gd-56) were more toxic as contact insecticides than the derivatives of thiophosphoric acid. Of the two amidoesters named above, against bugs of vrednii cherepashki, compound Gd-56, containing a diethylamido group, was twice as toxic as compound Gd-55, containing a dimethylamido group. No difference between the latter compounds appeared against the larvae of muchnistyi chervets but with other compounds (Gd-50 and Gd-52, Gd-53 and Gd-54) a certain tendency for a higher toxicity was noticed on replacement of a dimethylamide group by a diethylamide group.

A laboratory study of the systemic action of the compounds was made on autumn bugs of vrednii cherepashki fed on grain sprouts grown from grain wetted with 0.6% emulsions and also arachnoid mites (Tetranychus urticae Koch.) by spraying bean plants. In these experiments, bean plants populated by mites were sprayed with emulsions of 0.05% concentration. The results of the experiments are expressed in mortality (in %) of bugs of vrednii cherepashki on the fifth day after implantation on three-day old shoots and in the fall in the number of mites as a percentage of the original number with a correction for the control (on the counting days).

The data obtained are presented in Table 3, which shows that certain amidoesters of thiophosphoric and dithiophosphoric acids were active systemic acaricides. Of the substances containing the diethylamide grouping, compounds Gd-54 and Gd-56 were toxic to mites. On plants sprayed with emulsions of these compounds, a considerable fall in the number of mites was produced during a total of 20 days observation. In the experiments carried out, the compounds Gd-54 and Gd-56 were similar in action against mites but neither was as good as Mercaptophos; compound Gd-52 was characterized by very weak action.

Amidoesters containing the dimethylamido grouping (Gd-50, Gd-53 and Gd-55) on the whole were the least active acaricides, and the substance of the thiol type, Gd-53, most toxic, but its thione isomer, Gd-50, was found to be completely inactive against mites.

Testing the amidoesters as systemic insecticides on bugs of vrednii cherepashki did not give successful results. The highest mortality of the bugs, obtained by using amidoesters of dithiophosphoric acid (Gd-55 and Gd-56), did not exceed 37.5 and 30% while under the action of the standard preparation M-74, the mortality of the insects reached 97.5%.

The tetramethyldiamides of thiophosphoric acid (Gd-64 and Gd-66) showed very weak action both on arachnoid mites and on the bugs of vrednii cherepashki.

Thus, on the basis of the material obtained it can be said that certain of the amidoesters obtained, such as Gd-53, Gd-54 and Gd-56, for example, are active systemic acaricides and deserve further study.

EXPERIMENTAL

Ethyl Dimethylamidochlorothionephosphate. Through a solution of 36 g (0.2 mole) of ethyl dichlorothionephosphate in 50 ml of absolute ether was passed a stream of dimethylamine (18 g, 0.4 mole) at -5-0°. The mixture was stirred at room temperature for 1 hour and then the dimethylamine hydrochloride removed, the ether evaporated and the residue vacuum distilled. We obtained 30.1 g (79%) of ethyl dimethylamidochlorothionephosphate.

B.p. 72-73° (3 mm), $n^{20}D$ 1.4972, d_4^{20} 1.2008, MR_D 45.74; calc. 46.05.

Literature data [1]: b.p. 69° (3 mm).

Ethyl Diethylamidochlorothionephosphate. To a solution of 36 g (0.2 mole) of ethyl dichlorothionephosphate in 130 ml of absolute ether was slowly added diethylamine (29.2 g, 0.4 mole) at -10 to -15°. The temperature was then slowly raised to that of the room and the mixture heated at 35° for 1 hour. The diethylamine hydrochloride was removed, the ether evaporated and the residue vacuum distilled. We obtained 20.8 g (48%) of ethyl diethylamidochlorothionephosphate:

B.p. 105-106° (10 mm), $n^{20}D$ 1.4931, d_4^{20} 1.1352, MR_D 55.29; calc. 55.27.

Found %: C 33.25, 33.18; H 7.05, 7.12; P 14.51, 14.63; $C_6H_{15}ONPSCl$. Calculated %: C 33.41; H 7.01; P 14.36.

Tetramethyldiamidochlorothiophosphate. a) Through a solution of 85 g (0.5 mole) of phosphorus thiotrichloride in 500 ml of absolute ether was passed a stream of dimethylamine (90 g, 2 moles) at 0-5°. The mixture was stirred at room temperature for 1 hour and then the dimethylamine hydrochloride removed, the ether evaporated and the residue vacuum distilled from a Claisen flask with a long reflux head. We obtained 51 g (56%) of tetramethyldiamidochlorothiophosphate.

B.p. 57-58° (1 mm), $n^{23}D$ 1.5229; b.p. 22° (from ligroin).

Literature data [14]: b.p. 90° (2.5 mm).

Found %: C 25.69, 25.61; H 6.51, 6.61; P 16.35, 16.56. $C_4H_{12}NPSCl$. Calculated %: C 25.74; H 6.48; P 16.61.

b) 26 g of tetramethyldiamidochlorophosphate [15] and 8.5 g of P_2S_5 were heated in a stream of nitrogen at 150-160° for 5 hours and then the mixture was vacuum distilled in a stream of nitrogen. We obtained 15 g of substance with b.p. 50-70° (8 mm). A second distillation yielded 11.6 g (43%) of tetramethyldiamidochlorothiophosphate with b.p. 52-53° (0.8 mm); and m.p. 21.5°. A mixed melting point with the substance obtained by method "a" was not depressed.

β-Mercaptodiethyl sulfide was obtained by the method of Frank and Smith [16]. 600 g of 40% hydrobromic acid, 106 g (1 mole) of β-hydroxydiethyl sulfide and 76 g (1 mole) of thiourea were boiled for 10 hours and then a solution of 120 g of sodium hydroxide in 300 ml of water was carefully added and the mixture heated in a stream of nitrogen for 3 hours. The upper oily layer was then separated, the lower layer extracted with ether and the ether extracts combined with the oily layer and dried with sodium sulfate. The ether was removed and the residue vacuum distilled. We obtained 81 g (66%) of β-mercaptodiethyl sulfide.

B.p. 69-70° (13 mm), $n^{20}D$ 1.5281, d_4^{20} 1.0381, MR_D 36.19; calc. 36.36.

Literature data [17]: b.p. 37° (0.6 mm).

O-Ethyl-O-β-ethylmercaptoethyldimethylamidothiophosphate (Gd-50). To 4 g (0.1 mole) of powdered sodium hydroxide was added 10.6 g (0.1 mole) of β-hydroxydiethyl sulfide and the mixture stirred for 15 minutes after which 50 ml of absolute benzene was added and 18.7 g (0.1 mole) of ethyl dimethylamidochlorothionephosphate then introduced slowly at +15°. The temperature was then raised to 70° and the mixture heated at this temperature for 1 hour. The sodium chloride was removed, the benzene evaporated and the residue vacuum distilled. We obtained 12.6 g (49%) of O-ethyl-O-β-ethylmercaptoethyldimethylamidothiophosphate:

B.p. 112-114° (2.5 mm), $n^{20}D$ 1.5015, d_4^{20} 1.1091, MR_D 68.52; calc. 68.93.

Found %: C 37.32, 37.52; H 7.94, 7.88; P 11.84, 11.57; S 24.83, 25.01. $C_8H_{20}O_2NPS_2$. Calculated %: C 37.33; H 7.83; P 11.76; S 24.92.

By an analogous method we obtained the two following preparations.

O-Ethyl-O-β-ethylmercaptoethyldiethylamidothiophosphate (Gd-52) in 24% yield:

B.p. 118-120° (2 mm), $n^{20}D$ 1.4972, d_4^{20} 1.0779, MR_D 77.54; calc. 78.17.

Found %: C 42.14, 42.28; H 8.39, 8.45; P 10.52, 10.63; S 22.97, 23.00. $C_{10}H_{24}O_2NPS_2$. Calculated %: C 42.08; H 8.48; P 10.85; S 22.47.

O-β-Ethylmercaptoethyltetramethyldiamidothiophosphate (Gd-64) in 50% yield:

B.p. 105-106° (1.5 mm), $n^{20}D$ 1.5151, d_4^{20} 1.1008, MR_D 70.25; calc. 70.23.

Found %: C 37.28, 37.44; H 8.33, 8.18; P 12.12, 12.08; S 25.11. $C_8H_{21}ON_2PS_2$. Calculated %: C 37.47; H 8.26; P 12.08; S 2501.

O-Ethyl-S-β-ethylmercaptoethyldimethylamidothiophosphate (Gd-53). 25.7 g (0.1 mole) of O-ethyl-O-β-ethylmercaptoethyldimethylamidothiophosphate was heated in a stream of nitrogen for 10 hours at 150-160° (until the refractive index ceased to change) and the isomerization product was vacuum distilled. We obtained 16.5 g (64%) of O-ethyl-S-β-ethylmercaptoethyldimethylamidothiophosphate:

B.p. 122-123° (2.5 mm), $n^{20}D$ 1.5100, d_4^{20} 1.1272, MR_D 68.28; calc. 68.64.

Found %: C 37.10, 37.23; H 7.76, 7.79; P 11.65, 11.83; S 24.86, 25.12. $C_8H_{20}O_2NPS_2$. Calculated %: C 37.33; H 7.83; P 11.76; S 24.92.

By an analogous method we obtained the two following preparations.

O-Ethyl-S-β-ethylmercaptoethyldiethylamidothiophosphate (Gd-54) in 61% yield:

B.p. 142-143° (3 mm), $n^{20}D$ 1.5046, d_4^{20} 1.0884, MR_D 77.51; calc. 77.87.

Found %: C 41.99, 42.00; H 8.41, 8.39; P 10.30, 10.35; S 23.05, 23.12. $C_{10}H_{24}O_2NPS_2$. Calculated %: C 42.08; H 8.48; P 10.85; S 22.47.

S-β-Ethylmercaptoethyltetramethyldiamidothiophosphate (Gd-66) in 72% yield:

B.p. 103-104° (1 mm), $n^{20}D$ 1.5208, d_4^{20} 1.1165, MR_D 69.90; calc. 69.93.

Found %: C 37.43, 37.64; H 8.29, 8.29; P 12.37, 12.19; S 24.97, 25.05. $C_8H_{20}ON_2PS_2$. Calculated %: C 37.47; H 8.20; P 12.08; S 25.01.

O-Ethyl-S-β-ethylmercaptoethyldimethylamidodithiophosphate (Gd-55). To sodium methylate, obtained from 2.3 g (0.1 g-at.) of sodium and 50 ml of anhydrous methyl alcohol, was added 12.2 g (0.1 mole) of β-mercaptodiethyl sulfide, then the alcohol was removed by distillation and 50 ml of anhydrous benzene added followed by 18.7 g (0.1 mole) of ethyl dimethylamidochlorothionephosphate in small portions. The mixture was heated for 1 hour at 70° then water added, the benzene layer separated, the aqueous layer extracted with ether, the ether extracts combined with the benzene layer and the mixture dried over sodium sulfate. After removal of the solvent, the residue was vacuum distilled. We obtained 11.5 g (42%) of O-ethyl-S-ethylmercaptoethyldimethylamidodithiophosphate:

B.p. 136-137° (2.5 mm), $n^{20}D$ 1.5501, d_4^{20} 1.1409, MR_D 76.36; calc. 76.31.

Found %: C 35.24, 35.26; H 7.42, 7.47; P 10.74, 11.04; S 35.11, 34.88. $C_8H_{20}ONPS_3$. Calculated %: C 35.18; H 7.37; P 11.33; S 35.18.

O-Ethyl-S-β-ethylmercaptoethyldiethylamidodithiophosphate (Gd-56) was obtained in 32% yield by a method analogous to that described above:

B.p. 133-134° (2 mm), $n^{20}D$ 1.5430, d_4^{20} 1.1113, MR_D 85.60; calc. 85.64.

Found %: C 39.89, 39.79; H 8.08, 7.98; P 10.54, 10.51; S 31.98, 32.15. $C_{10}H_{14}ONPS_3$. Calculated %: C 39.84; H 8.02; P 10.27; S 31.91.

SUMMARY

1. We synthesized a series of derivatives of O-ethyldialkylamidothiophosphoric, O-ethyldialkylamidodithiophosphoric and tetramethyldiamidothiophosphoric acids containing the β-ethylmercaptoethyl grouping.

2. It was shown that on heating tetramethyldiamidochlorophosphate with P_2S_5 replacement of the oxygen atom by sulfur occurred with the formation of tetramethyldiamidothiophosphate.

3. The compounds synthesized were tested in the laboratory as insecticides and acaricides on bugs of vrednii cherepashki, muchnistyi chervets and arachnoid mites.

4. Certain of the amidoesters of thiophosphoric and dithiophosphoric acids (Gd-53, Gd-54 and Gd-56) were found to be active systemic acaricides against arachnoid mites.

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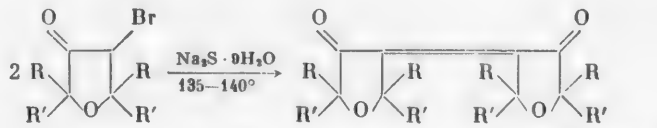
REACTIONS OF 4-BROMO- AND 4-HYDROXY-2,2,5,5-TETRA-ALKYLFURANIDONES-3

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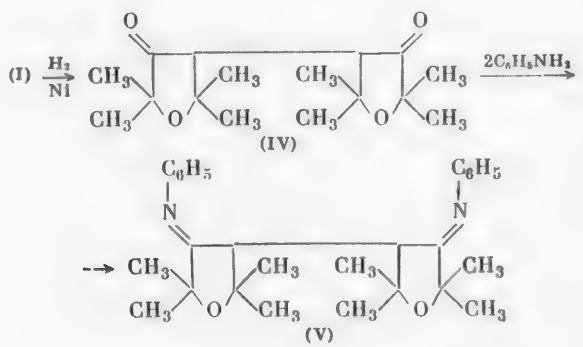
The low reactivity of the bromine in 4-bromo-2,2,5,5-tetraalkylfuranidones-3 sharply distinguishes these compounds from α-bromoketones of the aliphatic and alicyclic series. Thus, the bromine in 4-bromo-2,2,5,5-tetramethylfuranidone-3 is not replaced by a hydroxyl group (on hydrolysis with solutions of sodium and potassium carbonates), by iodine (on treatment with potassium iodide), by a thiocyano group (when heated with potassium thiocyanate) or by an amino group (when treated with ammonia); only the reaction with sodium cyanide gave a good yield of the corresponding nitrile [1, 2].

We attempted to use such halides for the synthesis of condensed systems containing furanidine and thiazole rings, but it was found that 4-bromo- and 4-chloro-2,2,5,5-tetramethylfuranidone-3 and also 4-bromo-2,2,5,5-bis-(pentamethylenefuranidone-3) would not react with thioacetamide, thiourea or ammonium thiocyanate. We were also unsuccessful in an attempt to replace bromine in these bromoketones by a mercapto group by the action of anhydrous sodium sulfide; when 4-bromo-2,2,5,5-tetraalkylfuranidones-3 were heated with crystalline sodium sulfide at 135-140°, hydrogen bromide was readily eliminated and condensation occurred with the formation of an unsaturated γ-diketone, containing two furanidine rings*.



(I) R = R′ = CH₃; (II) R = CH₃, R′ = C₂H₅; (III) R, R′ = =

Hydrogenation of (I) in the presence of Raney nickel yielded a saturated γ-diketone (IV), di-(2,2,5,5-tetramethylfuranidon-3-yl-4), which reacted with aniline to form the dianil (V).

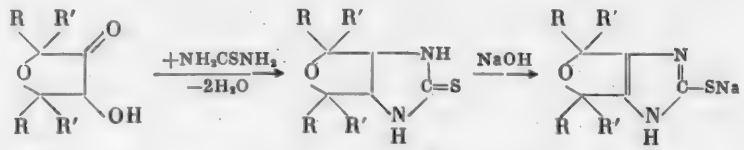


(IV)

(V)

*Compound (I) was obtained by Richet [2] (10% yield) by the hydrolysis of 4-bromo-2,2,5,5-tetramethylfuranidone-3 with sodium carbonate.

We then used 4-hydroxy-2,2,5,5-tetraalkylfuranidones-3 (VI)[3] for the synthesis of nitrogen heterocyclic systems containing a furanidine ring and established that the former reacted with thiourea giving the corresponding imidazolethione. By this method, from 4-hydroxy-2,2,5,5-tetramethyl- and 4-hydroxy-2,2,5,5-bispentamethylenefuranidones-3 we obtained 4,4,6,6-tetramethylfuranidino-(3, 4)-imidazolethione-2 (VII) and 4,4,6,6-bispentamethylenefuranidino-(3, 4)-imidazolethione-2 (VIII), respectively.

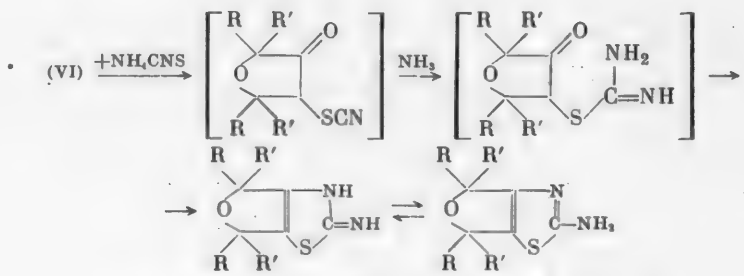


(VI)

(VII) R = R′ = CH3; (VIII) R, R = cyclohexane

Compounds (VII) and (VIII) did not dissolve in hydrochloric acid. Determination of the dissociation constant* of (VII) (pK_a = 11.2) showed that it did not have basic properties and was a weak acid. Similar weakly acidic properties are characteristic of all imidazolethiones-2, which react with strong bases in the form of 2-mercaptoimidazoles [5].

As is known, on reaction with thiourea and with ammonium thiocyanate, α-hydroxyketones of the aliphatic and aromatic series form imidazolethiones-2 [6]. 4-Hydroxy-2,2,5,5-tetraalkylfuranidones-3 (VI) reacted with ammonium thiocyanate differently and when they were fused with it at 150°, they gave the 2-amino-4,4,6,6-tetraalkylfuranidino-(3,4)-thiazoles (IX), (X) and (XI) in good yields:



(IX) R = R′ = CH3; (X) R, R′ = cyclopentane; (XI) R, R′ = cyclohexane

Compounds (IX), (X) and (XI) were isolated in the form of stable monohydrates as is characteristic of certain aminothiazoles of condensed structure [7]. The action of methyl iodide on compound (IX) yielded an iodomethylate, which did not contain water of crystallization. Potentiometric measurement of the dissociation constant of compound (IX) showed that it was amphoteric with the basic properties predominating over the acid ones: pK_b = 11.6 and pK_d = 12.13; consequently this compound could react both in the amine and in the imine forms.

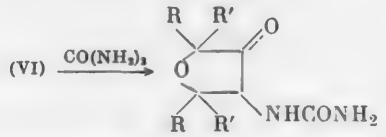
The predominance of the basic properties was confirmed by the fact that compounds (IX), (X) and (XI) dissolved in dilute hydrochloric acid and were precipitated from the hydrochloric acid solution by the addition of 2 N sodium carbonate solution.

As regards the mechanism of 2-amino-4,4,6,6-tetraalkylfuranidino-(3,4)-thiazole formation, the reaction apparently proceeds through the following stages: by reaction with ammonium thiocyanate, 4-thiocyano-2,2,5,5-tetraalkylfuranidones-3 were obtained first and these then reacted with ammonia, formed by thermal dissociation of ammonium thiocyanate, giving 2-amino-4,4,6,6-tetraalkylfuranidino-(3,4)-thiazoles.**

*The dissociation constant was determined by a method which we described previously [4].

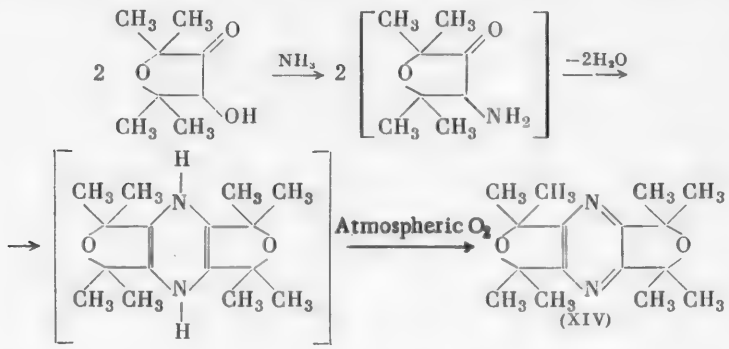
**The formation of aminothiazoles from thiocyanoketones and ammonia has been described in the literature [8].

As already stated, the interaction of 4-hydroxy-2,2,5,5-tetraalkylfuranidones-3 (VI) with thiourea was accompanied by the closure of the new ring and led to 4,4,6,6-tetraalkylfuranidino-(3,4)-imidazolethiones-2 (VII) and (VIII). The reaction with urea in glacial acetic acid proceeded with the elimination of only one water molecule and led to the formation of the substituted ureas 2,2,5,5-tetramethylfuranidon-3-yl-4-carbamide (XII) and 2,5-dimethyl-2,5-diethylfuranidon-3-yl-4-carbamide (XIII) from 4-hydroxy-2,2,5,5-tetramethyl- and 4-hydroxy-2,5-dimethyl-2,5-diethylfuranidones-3, respectively.



(XII) $R = R' = CH_3$; (XIII) $R = CH_3$, $R' = C_2H_5$.

As a side product of the reaction of urea and also of thiourea with 4-hydroxy-2,2,5,5-tetramethylfuranidone-3 (VI) we obtained 2,2,4,4-6,6,8,8-octamethyldifuranidino-(3,4)-pyrazine (XIV). This compound was formed as a result of the following series of reactions: 1) amination of 4-hydroxy-2,2,5,5-tetramethylfuranidone-3 by ammonia, formed by thermal decomposition of urea (or thiourea), and 2) condensation of the intermediate 4-amino-2,2,5,5-tetramethylfuranidone-3 into 2,2,4,4,6,6,8,8-octamethyldifuranidino-(3,4)-1,5-dihydropyrazine, which was oxidized by atmospheric oxygen to 2,2,4,4,6,6,8,8-octamethyldifuranidino-(3,4)-pyrazine (XIV):



We also obtained difuranidino-(3,4)-pyrazines by boiling 4-hydroxy-2,2,5,5-tetramethylfuranidone-3 and 4-hydroxy-2,2,5,5-bistetramethylenefuranidone-3 with ammonium acetate in glacial acetic acid.

Thus, 4-hydroxy-2,2,5,5-tetraalkylfuranidones-3, which are readily obtained by reduction of 4-isonitroso-2,2,5,5-tetraalkylfuranidones-3 with zinc in acetic acid [3], were found to be suitable for the synthesis of condensed nitrogen-containing heterocyclic systems including a furanidine ring, which are inaccessible by other methods, namely furanidino-(3,4)-imidazolethiones-2, 2-aminofuranidino-(3,4)-thiazoles and difuranidino-(3,4)-pyrazines.

EXPERIMENTAL

4-(2,2,5,5-Tetramethylfuranidon-3-ylidene-4)-2,2,5,5-tetramethylfuranidone-3 (I). A mixture of 5 g (0.02 mole) of 4-bromo-2,2,5,5-tetramethylfuranidone-3 and 5 g (0.02 mole) of crystalline sodium sulfide was heated for 2 hours under reflux on an oil bath at 130-140° and then cooled and poured into 100 ml of water. The yellow crystalline precipitate was collected and washed with water. We obtained 1.26 g (40%) of product; the m.p. was 137-137.5° (from alcohol).

Found %: C 68.24, 68.36; H 8.75, 8.74. $C_{16}H_{24}O_4$. Calculated %: C 68.54; H 8.63.

Literature data: m.p. 137° [2].

4-(2,5-Dimethyl-2,5-diethylfuranidon-3-ylidene-4)-2,5-dimethyl-2,5-diethylfuranidone-3 (II). A mixture of 25 g (0.1 mole) of 4-bromo-2,5-dimethyl-2,5-diethylfuranidone-3 and 24 g (0.1 mole) of crystalline

sodium sulfide was heated as described above poured into 100 ml of water and repeatedly extracted with ether. After removal of the ether from the calcium chloride dried extracts, we obtained 7.5 g (50%) of a yellow oil:

B.p. 148-149° (5 mm), $n^{20}D$ 1.4827, d_4^{20} 1.000, MR_D 96.02. $C_{20}H_{32}O_4F$. Calc. MR_D 93.00; error + 3.02.

Found %: C 71.34; H 9.66. $C_{20}H_{32}O_4$. Calculated %: C 71.39; H 9.59.

4-(2,2,5,5-Bispentamethylenefuranidon-3-ylidene-4)-2,2,5,5-bispentamethylenefuranidone-3 (III). A mixture of 4.5 g (0.015 mole) of 4-bromo-2,2,5,5-bispentamethylenefuranidone-3 and 5 g (0.02 mole) of crystalline sodium sulfide was heated as described above at 110-120°, poured into 50 ml of water and treated as described in (I). We obtained 2.0 g (66%) of bright yellow crystals with m.p. 203-203.5° (from anhydrous alcohol).

Found %: C 76.51, 76.41; H 9.26, 9.34. $C_{28}H_{40}O_4$. Calculated %: C 76.32; H 9.15.

Di-(2,2,5,5-tetramethylfuranidon-3-yl-4) (IV). 1 g (0.0036 mole) of the unsaturated γ-diketone (I) was dissolved in 120 ml of anhydrous alcohol and hydrogenated in the presence of Raney nickel with shaking in the cold. It absorbed 80 ml of hydrogen (STP); the calculated amount of hydrogen was 80 ml (STP). We obtained 1 g of compound (IV) (quantitative yield). The white crystals had m.p. 121-121.5° (from dilute alcohol).

Found %: C 68.39, 68.23; H 9.47, 9.51. $C_{16}H_{26}O_4$. Calculated %: C 68.05; H 9.28.

Dianil of Di-(2,2,5,5-tetramethylfuranidon-3-yl-4) (V). To a mixture of 1 g (0.003 mole) of (IV) and 2 ml of aniline was added 0.5 g of anhydrous zinc chloride. The mixture was boiled for 10 minutes and decomposed with 50 ml of cold water. The precipitate was collected and recrystallized from cyclohexane. We obtained 1 g (65%) of dianil (V) as a white crystalline substance with m.p. 260° (decomp.).

Found %: N 6.54, 6.64. $C_{28}H_{36}O_2N_2$. Calculated %: N 6.48.

4,4,6,6-Tetramethylfuranidino-(3,4)-imidazolethione-2 (VII). A solution of 1 g (0.0064 mole) of 4-hydroxy-2,2,5,5-tetramethylfuranidone-3 and 0.8 g (0.01 mole) of thiourea in 3 ml of glacial acetic acid was boiled for 5 hours in a flask with a reflux condenser and poured into 20 ml of cold water. The crystals were collected and washed with water. We obtained 0.8 g (64%) of product with m.p. 292-293° (from cyclohexane).

Found %: C 54.61, 54.47; H 7.24, 7.05; N 14.08, 14.41. $C_9H_{14}ON_2S$. Calculated %: C 54.51; H 7.12; N 14.13.

(VII) was a white crystalline substance, which dissolved readily in alcohol and acetic acid, but was insoluble in ether, water and hydrochloric acid.

4,4,6,6-Bispentamethylenefuranidino-(3,4)-imidazolethione-2 (VIII). A mixture of 1.0 g (0.0042 mole) of 4-hydroxy-2,2,5,5-bispentamethylenefuranidone-3, 0.4 g (0.0052 mole) of thiourea and 1.5 ml of glacial acetic acid was boiled for 3 hours in a flask with a reflux condenser and poured into 20 ml of water. We obtained 0.6 g (51%) of product with m.p. 300-300.5° (from aqueous alcohol).

Found %: C 64.64; H 8.01; N 10.13, 10.12. $C_{15}H_{22}ON_2S$. Calculated %: C 64.71; H 7.97; N 10.06.

2-Amino-4,4,6,6-tetramethylfuranidino-(3,4)thiazole (IX). A mixture of 1 g (0.0064 mole) of 4-hydroxy-2,2,5,5-tetramethylfuranidone-3 with 0.76 g (0.01 mole) of ammonium thiocyanate was placed into a round-bottomed flask preliminarily heated to 100° on a Wood's metal bath and rapidly heated to 120°. The reaction mixture melted and on heating to 140° (over a period of 2-3 minutes) a vigorous reaction began, accompanied by foaming and evolution of water vapor (1-2 minutes) and the mixture then solidified to a light yellow porous mass. The reaction product was ground first with absolute ether and then with water (until the reaction for a thiocyanate ion disappeared). Drying the residue in a vacuum desiccator yielded 1.0 g (73%) of the hydrate of 2-amino-4,4,6,6-tetramethylfuranidino-(3,4)-thiazole (IX) with m.p. 252-253° (from alcohol); the white crystals were soluble in hot alcohol and dilute hydrochloric acid, but insoluble in water and ether.

Found %: C 49.96, 50.08; H 7.50, 7.60; N 12.60, 12.49. $C_9H_{14}ON_2S \cdot H_2O$. Calculated %: C 49.97; H 7.46; N 12.95.

Iodomethylate of 2-Amino-4,4,6,6-tetramethylfuranidino-(3,4)-thiazole was obtained by heating 0.5 g (0.0023 mole) of (IX) with 0.5 ml (0.0081 mole) of methyl iodide in a sealed tube on a water bath for 2 hours. Evaporation of the methyl iodide and washing with ether yielded 0.4 g (51%) of product with m.p. 170° (reprecipitation from anhydrous alcohol with ether); the white needles rapidly became yellow in light.

Found %: C 35.48, 35.26; H 5.10, 5.08; N 7.98, 7.92. $C_{10}H_{17}ON_2SI$. Calculated %: C 35.32; H 5.04; N 8.23.

2-Amino-4,4,6,6-bistetramethylenefuranidino-(3,4)-thiazole (X). 1.0 g (0.0049 mole) of 4-hydroxy-2,2,5,5-bistetramethylenefuranidone-3 and 0.76 g (0.01 mole) of ammonium thiocyanate were heated for 10 minutes at 118-120° and the mass treated with ether and water. We obtained 1.0 g (79%) of (X) with m.p. 275-276° (from alcohol); the white crystals dissolved in alcohol and dilute hydrochloric acid and were insoluble in water and ether.

Found %: C 57.97; H 7.57; N 10.28. $C_{13}H_{18}ON_2S \cdot H_2O$. Calculated %: C 58.16; H 7.52; N 10.44.

2-Amino-4,4,6,6-bispentamethylenefuranidino-(3,4)-thiazole (XI). A finely ground mixture of 1 g (0.0042 mole) of 4-hydroxy-2,2,5,5-bispentamethylenefuranidone-3 and 0.76 g (0.01 mole) of ammonium thiocyanate was heated for 5 minutes at 150°. The cooled mass was ground and washed with ether and water. We obtained 0.9 g (72.5%) of (XI) with m.p. 306-306.5° (from alcohol); the white crystals dissolved readily in hot alcohol and hydrochloric acid and were insoluble in water and ether.

Found %: C 60.83, 61.10; H 8.32, 8.51; N 9.28, 9.34. $C_{15}H_{22}ON_2S \cdot H_2O$. Calculated %: C 60.78; H 8.16; N 9.45.

2,2,5,5-Tetramethylfuranidon-3-yl-4-carbamide (XII). A solution of 0.5 g (0.0032 mole) of 4-hydroxy-2,2,5,5-tetramethylfuranidone-3 and 0.36 g (0.006 mole) of urea in 5 ml of glacial acetic acid was boiled for 5 hours under reflux and the mixture poured into 20 ml of cold water. The precipitate was collected and washed with ether. We obtained 0.4 g (62%) of product with m.p. 209-209.5° (from alcohol); the white crystals were soluble in alcohol and insoluble in water and ether.

Found %: C 54.20, 54.13; H 8.35, 8.33; N 13.98, 14.15. $C_9H_{16}O_3N_2$. Calculated %: C 53.98; H 8.05; N 13.99.

2,5-Dimethyl-2,5-diethylfuranidon-3-yl-4-carbamide (XIII). A mixture of 1.0 g (0.0055 mole) of 4-hydroxy-2,5-dimethyl-2,5-diethylfuranidone-3, 0.72 g (0.012 mole) of urea and 1 ml of glacial acetic acid was boiled for 1 hour under reflux and poured into 20 ml of cold water. The precipitate was collected and washed with ether. We obtained 0.9 g (73%) of product with m.p. 190.5-191.5° (from aqueous alcohol).

Found %: C 57.28, 57.19; H 9.07, 8.98; N 11.77, 12.00. $C_{11}H_{20}O_3N_2$. Calculated %: C 57.87; H 8.83; N 12.27.

2,2,4,4,6,6,8,8-Octamethyldifuranidino-(3,4)-pyrazine (XIV). To ammonium acetate (from 2 g of ammonium carbonate in 2 ml of glacial acetic acid) was added 0.2 g (0.0012 mole) of 4-hydroxy-2,2,5,5-tetramethylfuranidone-3. The mixture was heated for 2 hours under reflux, cooled and poured into 20 ml of water. We obtained 0.05 g (30%) of product with m.p. 235-235.5° (from alcohol).

Found %: C 69.58, 69.74; H 8.86, 8.92; N 10.49, 10.60. $C_{16}H_{24}O_2N_2$. Calculated %: C 69.53; H 8.75; N 10.14.

The melting point was not depressed by admixture with samples of 2,2,4,4,6,6,8,8-octamethyldifuranidino-(3,4)-pyrazines, obtained as side products in the reaction of 4-hydroxy-2,2,5,5-tetramethylfuranidone-3 with urea and thiourea.

2,2,4,4,6,6,8,8-Tetra-(tetramethylene)-difuranidino-(3,4)-pyrazine. To ammonium acetate (from 6 g of ammonium carbonate in 6 ml of glacial acetic acid) was added 1 g (0.005 mole) of 4-hydroxy-2,2,5,5-bistetramethylenefuranidone-3. The mixture was boiled for 3 hours under reflux, cooled and poured into 20 ml of water. The precipitate was collected, washed with water, dried in a vacuum desiccator and boiled with 20 ml of anhydrous alcohol; the insoluble part was collected and recrystallized from a large amount of anhydrous alcohol. We obtained 0.2 g (22%) of product with m.p. 262-262.5°.

Found %: C 75.85, 75.79; H 8.75, 8.70; N 6.85, 7.09. $C_{24}H_{32}O_2N_2$. Calculated %: C 75.75; H 8.49; N 7.36.

SUMMARY

1. Under the action of sodium sulfide, 4-bromo-2,2,5,5-tetraalkylfuranidones-3 formed unsaturated γ-diketones containing two furanidine rings and the hydrogenation of these led to the corresponding saturated γ-diketones.

2. In contrast to acyloins of the aliphatic, alicyclic and aromatic series, 4-hydroxy-2,2,5,5-tetraalkylfuranidones-3 reacted with thiourea and ammonium thiocyanate to form different reaction products, namely 4,4,6,6-tetraalkylfuranidino-(3,4)-imidazolethiones-2 and 2-amino-4,4,6,6-tetraalkylfuranidino-(3,4)-thiazoles, respectively.

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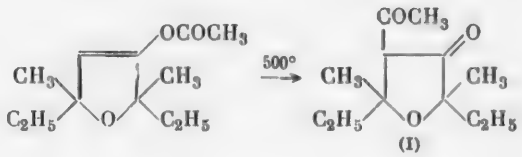
* Original Russian pagination. See C. B. Translation.

4-ACETYL-2,2,5,5-TETRAALKYLFURANIDONES-3

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In previous work we showed that 4-acetyl-2,2,5,5-tetramethylfuranidone-3 was formed by thermal isomerization of the enol acetate of 2,2,5,5-tetramethylfuranidone-3 [1]. In the present work we attempted to use this method for the synthesis of higher homologs of 4-acetyl-2,2,5,5-tetraalkylfuranidones-3. We established that when the enol acetate of 2,5-dimethyl-2,5-diethylfuranidone-3 was passed through a quartz tube packed with glass wool and heated to 500°, it was isomerized into 4-acetyl-2,5-dimethyl-2,5-diethylfuranidone-3 in 15.6% yield.



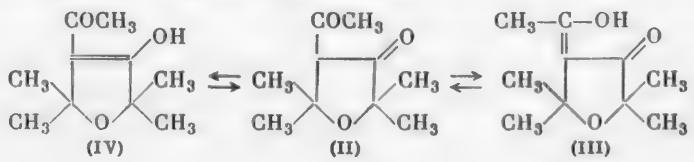
(I)

Attempts to obtain 4-acetyl-2,2,5,5-bispentamethylene furanidone-3 by thermal isomerization of the enol acetate of 2,2,5,5-bispentamethylenefuranidone-3 did not lead to positive results: the condensates obtained at 500-540° were shown to contain a β-diketone qualitatively only by the intense color with ferric chloride solution. Thus increasing the radicals in positions 2 and 5 of the starting enol acetates of 2,2,5,5-tetraalkylfuranidones-3 sharply lowered the yields of their thermal isomerization products, namely the corresponding 4-acetyl-2,2,5,5-tetraalkylfuranidones-3. Despite this, the method remained the only one for the preparation of 4-acetyl-2,2,5,5-tetramethylfuranidone-3 and 4-acetyl-2,5-dimethyl-2,5-diethylfuranidone-3 since attempts to obtain the latter by ester condensation of appropriate ketones with ethyl acetate in the presence of sodium or sodamide did not give positive results.

It also seemed interesting to determine to what extent 4-acetyl-2,2,5,5-tetraalkylfuranidones-3 and, in particular, their most accessible representative, 4-acetyl-2,2,5,5-tetramethylfuranidone-3, showed the characteristic properties of β-dicarbonyl compounds [2].

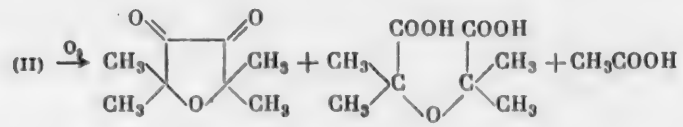
4-Acetyl-2,2,5,5-tetraalkylfuranidones-3 gave an intense color with ferric chloride solution and formed crystalline copper salts, in which form they were isolated from the thermal isomerization products [1]. A determination of the percentage content of the enol form by Meyer's method [3] showed that 4-acetyl-2,2,5,5-tetramethylfuranidone-3 was 99% enolized. Such a high content of the enol form is characteristic of all β-diketones with a large hydrocarbon radical adjacent to the carbonyl group [4].

The tautomeric form of 4-acetyl-2,2,5,5-tetramethylfuranidone-3 (II) could have been either the hydroxyketone with a semicyclic double bond (III) or the hydroxyketone of the dihydrofuran series (IV).



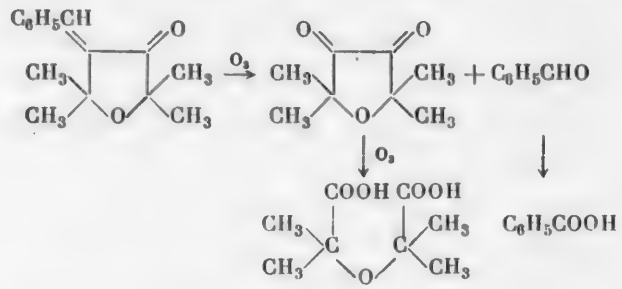
(IV) (II) (III)

To determine the direction of enolization of 4-acetyl-2,2,5,5-tetramethylfuranidone-3, we ozonized it and obtained 2,2,5,5-tetramethylfuranidinedione-3,4 and tetramethyldiglycolic and acetic acids.



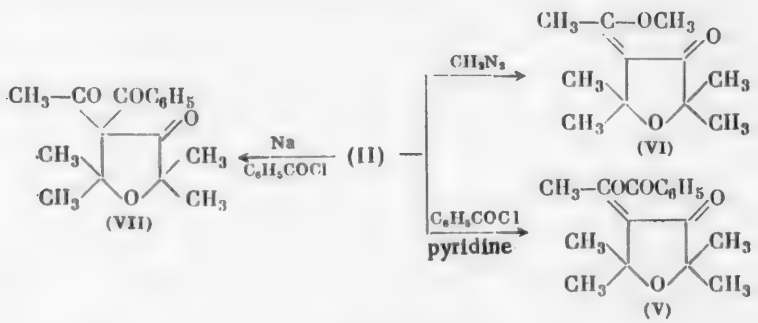
Tetramethyldiglycolic acid was obtained as a result of further oxidation of 2,2,5,5-tetramethylfuranidinedione-3,4 by ozone, as was confirmed both by literature analogies [5] and by the fact that we obtained tetramethyldiglycolic acid by treating this α-diketone with ozone.

Ozonization proceeded similarly with 4-benzylidene-2,2,5,5-tetramethylfuranidone-3, i.e., a compound with an authentic semicyclic double bond, and at the beginning of the reaction a crimson color was observed indicating the formation of 2,2,5,5-tetramethylfuranidinedione-3,4; further treatment with ozone and processing the reaction products in the usual way yielded only benzoic and tetramethyldiglycolic acids.



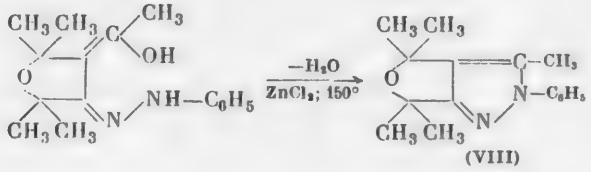
Thus, we established that the enolization of 4-acetyl-2,2,5,5-tetramethylfuranidone-3 (II) proceeded in the direction of the exocyclic carbonyl group and consequently the tautomeric form of such a β-diketone of the furanidine series is the hydroxyketone with a semicyclic double bond (III). Enolization toward the exocyclic carbonyl group is characteristic of β-diketones of similar structure; thus, it was established that the tautomeric form of benzoylcamphor is a hydroxyketone with a semicyclic double bond [6].

4-Acetyl-2,2,5,5-tetramethylfuranidone-3 (II) readily gave both O- and C-derivatives: the action of benzoyl chloride in pyridine gave the O-benzoate of the enol form (V) and methylation with diazomethane, the O-methyl ether (VI); treatment of the sodium salt of 4-acetyl-2,2,5,5-tetramethylfuranidone-3 with benzoyl chloride yielded 4-acetyl-4-benzoyl-2,2,5,5-tetramethylfuranidone-3 (VII).



On treating β-diketones with phenylhydrazine, hydrazine, hydroxylamine or semicarbazone, it is rarely possible to isolate phenylhydrazones, hydrazones, oximes or semicarbazones as they immediately cyclize into the corresponding heterocyclic compounds, namely phenylpyrazoles, pyrazoles, isoxazoles or amides of pyrazolecarboxylic acids [2]. 4-Acetyl-2,2,5,5-tetramethylfuranidone-3 behaved differently [1]: it formed a stable

hydrazone, oxime, semicarbazone and phenylhydrazone and the latter was not cyclized on distillation but only on fusion with zinc chloride at 150° did it form 1-phenyl-4,4,6,6,8-pentamethylfuranidino-(3,4)-pyrazole (VIII).



(VIII)

EXPERIMENTAL

4-Acetyl-2,5-dimethyl-2,5-diethylfuranidone-3 (I). 7 g (0.013 mole) of the enol acetate of 2,5-dimethyl-2,5-diethylfuranidone-3 [1] was passed at 500° at a rate of 3.57 ml/hr. through a quartz tube packed with glass wool (internal diameter 10 mm, length of heated section 100 mm), connected to a well-cooled receiver. Vacuum distillation of the isomerization product yielded 4 g of unchanged enol acetate of 2,5-dimethyl-2,5-diethylfuranidone-3. To the residue in the distillation flask was added a warm, saturated solution of copper acetate and the oil formed solidified after 12 hours standing. We obtained 0.54 g (15.6% calculated on the enol acetate reacted) of the copper salt of 4-acetyl-2,5-dimethyl-2,5-diethylfuranidone-3 with m.p. 146-147° (from aqueous alcohol).

Found %: C 58.85, 59.04; H 7.88, 7.94; Cu 13.72, 13.44. $C_{24}H_{38}O_6Cu$. Calculated %: C 59.29; H 7.88; Cu 13.08.

3.7 g (0.013 mole) of the copper salt of the diketone was decomposed with 20% sulfuric acid under a layer of ether. The ether layer was separated and the aqueous one extracted with ether. The ether extracts were washed with a 5% solution of sodium carbonate and dried with sodium sulfate. After removal of the ether we obtained 1.5 g (46%) of 4-acetyl-2,5-dimethyl-2,5-diethylfuranidone-3.

It gave an intense violet color with ferric chloride solution.

B.p. 103-105° (7 mm), $n^{22}D$ 1.4728, d_4^{20} 1.0152, MR_D 58.64. $C_{12}H_{20}O_3F$. Calculated: 58.13; EM_D +0.51.

Found %: C 68.23; H 9.70. $C_{12}H_{20}O_3$. Calculated %: C 67.89; H 9.50.

Ozonization of 4-Acetyl-2,2,5,5-tetramethylfuranidone-3. For a period of 1 hour 10 minutes, a fast stream of 5% ozone was passed into a solution of 2.02 g (0.01 mole) of the monohydrate of 4-acetyl-2,2,5,5-tetramethylfuranidone-3 [1] in 50 ml of anhydrous carbon tetrachloride, cooled to -20°. The bright crimson solution obtained was kept at 18° for 2 hours and then the solvent was removed in vacuum in the cold and the residue decomposed by 10 minutes boiling with 15 ml of water. The colorless, clear solution formed had a strong odor of acetic acid and showed an acid reaction (pH 1); the reaction with ferric chloride was negative. The solution was made alkaline with sodium carbonate solution to pH 12 and bright crimson 2,2,5,5-tetramethylfuranidinedione-3,4 was extracted from it with warm benzene; after removal of the benzene, the residue yielded 0.4 g (16.3%) of the phenylhydrazone of 2,2,5,5-tetramethylfuranidinedione-3,4 with m.p. 96-97°.

Found %: C 68.35, 68.11; H 7.56, 7.47; N 11.39, 11.45. $C_{14}H_{18}O_2N_2$. Calculated %: C 68.28; H 7.37; N 11.37.

The aqueous alkaline solution was evaporated to a volume of 15 ml and then acidification with concentrated hydrochloric acid yielded 1.4 g (74%) of tetramethyldiglycolic acid with m.p. 153-154° (from chloroform).

Literature data: m.p. 153-155° [7].

Found %: C 50.73, 50.67; H 7.62, 7.63. $C_8H_{14}O_5$. Calculated %: C 50.52; H 7.42.

Oxidation of 2,2,5,5-Tetramethylfuranidinedione-3,4 With Ozone. A fast stream of ozone was passed for 1 hour into a solution of 0.5 g (0.0032 mole) of 2,2,5,5-tetramethylfuranidinedione-3,4 [8] in 15 ml of carbon tetrachloride at 10° (the mixture was not decolorized during this time). Processing (as described above) yielded 0.1 g (17%) of tetramethyldiglycolic acid with m.p. 153-154° and we obtained 0.6 g (75%) of the phenylhydrazone of the original diketone with m.p. 95-97°.

Ozonization of 4-Benzylidene-2,2,5,5-tetramethylfuranidone-3. A fast stream of ozone was passed for 1 hour into a solution of 1 g (0.004 mole) of 4-benzylidene-2,2,5,5-tetramethylfuranidone-3 [7] in 30 ml of carbon tetrachloride at 10°. Processing (as described above) yielded 0.4 g (80%) of benzoic acid with m.p. 121-122° and 0.65 g (86%) of tetramethyldiglycolic acid with m.p. 153-155°. Mixed melting points with preparations obtained previously were not depressed.

4-Acetyl-4-benzoyl-2,2,5,5-tetramethylfuranidone-3 (VII). To a solution of 0.36 g (0.002 mole) of 4-acetyl-2,2,5,5-tetramethylfuranidone-3 in 5 ml of absolute ether was added 0.04 g (0.002 g-at.) of sodium. When the sodium had dissolved completely, 0.28 g (0.002 mole) of benzoyl chloride was added dropwise and the mixture boiled under reflux for 3 hours. The precipitate was removed and washed with absolute ether. After removal of the ether from the combined ether solutions, the residue crystallized. We obtained 0.53 g (90%) of product with m.p. 92-93° (after reprecipitation from alcohol with water).

Found %: C 71.29; H 7.38. $C_{17}H_{20}O_4$. Calculated %: C 70.81; H 6.99.

O-Benzoate of 4-Acetyl-2,2,5,5-tetramethylfuranidone-3 (V). 0.28 g (0.002 mole) of benzoyl chloride was added dropwise to a solution of 0.36 g (0.002 mole) of 4-acetyl-2,2,5,5-tetramethylfuranidone-3 in 1 ml of dry pyridine. After 3 hours the reaction mixture was poured into 40 ml of cold water and the precipitated crystals collected. We obtained 0.55 g (95%) of product with m.p. 89-89.5° (after reprecipitation from alcohol with water).

A mixture with 4-acetyl-4-benzoyl-2,2,5,5-tetramethylfuranidone-3 melted with depression at 65-67°.

Found %: C 71.20, 71.00; H 7.25, 7.20. $C_{17}H_{20}O_4$. Calculated %: C 70.81; H 6.99.

Methyl Ether of 4-Acetyl-2,2,5,5-tetramethylfuranidone-3 (VI). To a solution of 1.8 g (0.01 mole) of 4-acetyl-2,2,5,5-tetramethylfuranidone-3 in 200 ml of ether at 0° was added excess of an ether solution of diazomethane and the solution left at 18° for 7 days. After removal of the ether, distillation of the residue in vacuum yielded 0.7 g (35%) of product.

B.p. 73-75° (2 mm), m.p. 42° (from ligroin).

Found %: C 66.20; H 9.20. $C_{11}H_{18}O_3$. Calculated %: C 66.66; H 9.14.

Hydrazone of 4-Acetyl-2,2,5,5-tetramethylfuranidone-3. To a solution of 3 g (0.016 mole) of diketone in 50 ml of absolute ether was added 1.5 ml (0.03 mole) of hydrazine hydrate; the mixture was shaken and left for 3 hours at 18°. Removal of the water and evaporation of the ether yielded 3.1 g (95%) of product with m.p. 121-122° (from ligroin).

Found %: N 14.34, 13.97. $C_{10}H_{18}O_2N_2$. Calculated %: N 14.13.

Oxime of 4-Acetyl-2,2,5,5-tetramethylfuranidone-3. From 1.84 g (0.01 mole) of diketone and 0.7 g (0.01 mole) of hydroxylamine hydrochloride in 5 ml of dry pyridine and 5 ml of anhydrous alcohol, by boiling the mixture for 2 hours, evaporating it to dryness and recrystallizing the residue, we obtained 2 g (quantitative yield) of product with m.p. 145-146° (from cyclohexane).

Found %: C 60.32, 60.47; H 8.82, 8.79; N 7.14, 7.18. $C_{10}H_{17}O_3N$. Calculated %: C 60.28; H 8.60; N 7.03.

1-Phenyl-4,4,6,6,8-pentamethylfuranidino-(3,4)-pyrazole (VIII). 0.5 g (0.0018 mole) of the phenylhydrazone of 4-acetyl-2,2,5,5-tetramethylfuranidone-3 [1] was ground with 0.5 g of anhydrous zinc chloride and the mixture fused (150° in the bath) and cooled. The glassy mass was ground with 10 ml of water and the insoluble residue collected and dissolved in 10 ml of acetone. The acetone solution was filtered through activated charcoal and poured into 50 ml of cold water. The precipitated oil crystallized on scratching the beaker. 0.44 g (93%) of product with m.p. 70-70.5° (from aqueous alcohol) was obtained.

Found %: C 75.45; H 7.95; N 11.13, 11.20. $C_{16}H_{20}ON_2$. Calculated %: C 74.96; H 7.86; N 10.93.

SUMMARY

1. Isomerization of enol acetates of 2,2,5,5-tetraalkylfuranidones-3 may be used as a method of synthesizing 4-acetyl-2,2,5,5-tetraalkylfuranidones-3 when methyl or ethyl radicals are in positions 2 and 5.

2. 4-Acetyl-2,2,5,5-tetramethylfuranidone-3 is enolized to a high degree in the direction of the exocyclic carbonyl group; depending on the conditions, it forms C- and O-derivatives on acylation.

3. In reactions leading to condensed heterocyclic systems, for example to 1-phenyl-4,4,6,6,8-pentamethylfuranidino-(3,4)-pyrazole, β-diketones of the 2,2,5,5-tetraalkylfuranidine series require considerably more drastic conditions than aliphatic or alicyclic β-diketones.

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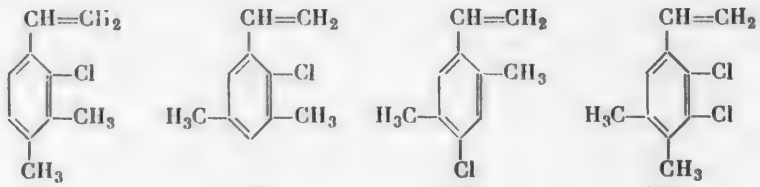
SYNTHESIS OF CHLORO-SUBSTITUTED DIMETHYLSTYRENES

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Until recently, tri- and tetrasubstituted styrenes remained almost unstudied. There was only patent data on the polymerization of trichlorostyrenes and tetrachlorostyrenes [1] without detailed descriptions of their preparation. It seemed interesting to synthesize halo-substituted vinylxylenes.

We had previously prepared [2] styrene derivatives containing simultaneously halogen atoms and a methyl group in the benzene ring. Extending these investigations, we synthesized chloro-substituted dimethylstyrenes, namely 2-chloro-3,4-dimethylstyrene (I), 2-chloro-3,5-dimethylstyrene (II), 4-chloro-2,5-dimethylstyrene (III) and 2,3-dichloro-4,5-dimethylstyrene (IV).



(I) (II) (III) (IV)

The synthesis of chloro-substituted dimethyl styrenes may be represented by the following scheme:

$$(CH_3)_2C_6H_4 \xrightarrow[AlCl_3+S_2Cl_2]{SO_2Cl_2} (CH_3)_2C_6H_3Cl \xrightarrow[AlCl_3]{CH_3COCl} (CH_3)_2C_6H_2ClCOCH_3 \xrightarrow{H} \longrightarrow (CH_3)_2C_6H_2ClCH(OH)CH_3 \xrightarrow[KHSO_4]{-H_2O} (CH_3)_2C_6H_2ClCH{=}CH_2$$

EXPERIMENTAL

Synthesis of 2-Chloro-3,4-dimethylstyrene. The starting o-xylene was chlorinated in the nucleus with sulfuryl chloride in the presence of aluminum chloride and sulfur monochloride by Silberrad's method [3]. The chlorinating agent, 140 g of sulfuryl chloride and 1.5 g of sulfur monochloride, was added over a period of 45 minutes to 106 g (1 mole) of o-xylene and 5 g (0.04 mole) of anhydrous aluminum chloride at 70°. The mixture was then heated for 30 minutes at 70° and poured into a large volume of water. Washing, drying and distillation gave a 65% yield of 3-chloro-1,2-dimethylbenzene as a colorless liquid:

B.p. 187-190°, $n^{20}D$ 1.5300.

Found %: Cl 25.1. C_8H_9Cl. Calculated %: Cl 25.2.

Acetylation of 3-chloro-1,2-dimethylbenzene (1 mole) with acetyl chloride (1.1 mole) in the presence of anhydrous aluminum chloride (1.1 mole) gave a 69% yield of 2-chloro-3,4-dimethylacetophenone:

B.p. 115° (1-2 mm), $n^{18}D$ 1.5512, MR_D 50.95; calc. 49.66.

Found %: Cl 18.61. $C_{10}H_{11}OCl$. Calculated %: Cl 19.45.

Reduction of 2-chloro-3,4-dimethylacetophenone (0.5 mole) with aluminum isopropoxide (prepared from 15 g of aluminum) in anhydrous isopropyl alcohol gave a 44% yield of 2-chloro-3,4-dimethylphenylmethylcarbinol as a colorless, viscous liquid:

B.p. 140° (7-8 mm), $n^{18.5}D$ 1.5470, d_4^{20} 1.1417, MR_D 51.01; calc. 51.27.

Dehydration of the carbinol over potassium bisulfate by the usual method yielded the monomer of 2-chloro-3,4-dimethylstyrene as a clear, colorless liquid with the odor of styrene:

B.p. 74° (1 mm), $n^{20}D$ 1.5634, d_4^{20} 1.0795, MR_D 50.12; calc. 49.17.

Found %: Cl 21.32. $C_{10}H_{11}Cl$. Calculated %: Cl 21.04.

Synthesis of 2-Chloro-3,5-dimethylstyrene. Chlorination of m-xylene by Silberrad's method [3] gave 2-chloro-1,5-dimethylbenzene in 68% yield and this had b.p. 187-188° and $n^{20}D$ 1.5232.

Acetylation of 2-chloro-1,5-dimethylbenzene gave a 76% yield of 2-chloro-3,5-dimethylacetophenone as a clear, colorless liquid:

B.p. 125-128° (10 mm), $n^{20}D$ 1.5511, d_4^{20} 1.1750, MR_D 49.87; calc. 49.66.

Reduction of 2-chloro-3,5-dimethylacetophenone gave a 70% yield of the carbinol as a clear, viscous liquid with b.p. 137-139° (6 mm), $n^{20}D$ 1.5449.

Dehydration of the carbinol gave a 60% yield of the monomer of 2-chloro-3,5-dimethylstyrene as a clear, colorless liquid with the odor of styrene:

B.p. 83-84° (1 mm), $n^{20}D$ 1.5600, d_4^{20} 1.0713, MR_D 50.26; calc. 49.18.

Synthesis of 4-Chloro-2,5-dimethylstyrene. Chlorination of p-xylene by Silberrad's method [3] gave a 66% yield of 3-chloro-1,4-dimethylbenzene:

B.p. 180-185°, $n^{20}D$ 1.5236.

Found %: Cl 24.65. C_8H_8Cl. Calculated %: Cl 25.2.

By acetylating 3-chloro-1,4-dimethylbenzene we obtained an 80% yield of 4-chloro-2,5-dimethylacetophenone as white crystals:

m.p. 27°, b.p. 127° (9 mm), $n^{30}D$ 1.5460, d_4^{20} 1.1740, MR_D 49.32; calc. 49.66.

Found %: Cl 19.53. $C_{10}H_{11}OCl$. Calculated %: Cl 19.45.

Reduction of 4-chloro-2,5-dimethylacetophenone gave the carbinol as white crystals.

m.p. 34°, b.p. 134° (1 mm), $n^{35}D$ 1.5465, d_4^{20} 1.1430, MR_D 51.14; calc. 51.27.

By dehydration of the carbinol over potassium bisulfate we obtained the monomer of 4-chloro-2,5-dimethylstyrene as a clear, colorless liquid with the smell of styrene; the yield was 54%:

B.p. 64° (1 mm), $n^{20}D$ 1.5603, d_4^{20} 1.0730, MR_D 50.19; calc. 49.17.

Found %: Cl 21.41. $C_{10}H_{11}Cl$. Calculated %: Cl 21.32.

Synthesis of 2,3-Dichloro-4,5-dimethylstyrene. 3,4-Dichloro-1,2-dimethylbenzene was prepared similarly to the monochlorodimethylbenzenes by chlorination of o-xylene by Silberrad's method [3], but at a higher temperature (85-90°); the yield was 48%. 3,4-Dichloro-1,2-dimethylbenzene was a clear, colorless liquid:

B.p. 228-231°, freezing point 14.5°, $n^{20}D$ 1.5541, d_4^{20} 1.2440, MR_D 45.18; calc. 44.48.

Acetylation of 3,4-dichloro-1,2-dimethylbenzene gave 2,3-dichloro-4,5-dimethylacetophenone. The yield was 69%:

B.p. 137° (4-5 mm), $n^{20}D$ 1.5650, d_4^{20} 1.2768, MR_D 55.22; calc. 54.52.

Found %: Cl 32.68. $C_{10}H_{10}OCl_2$. Calculated %: Cl 32.72.

By reduction of the ketone we obtained a 70% yield of 2,3-dichloro-4,5-dimethylphenylmethylcarbinol as fine, white crystals:

B.p. 125-135° (4-5 mm), m.p. 66-68°.

Found %: Cl 31.60. $C_{10}H_{12}OCl_2$. Calculated %: Cl 32.42.

Dehydration of the carbinol over potassium bisulfate yielded the monomer of 2,3-dichloro-4,5-dimethylstyrene as a colorless liquid with the characteristic odor of styrene:

B.p. 97-102° (1 mm), n_D^{20} 1.5805, d_4^{20} 1.2234, MR_D 54.76; calc. 54.05.

Found %: Cl 35.40. $C_{10}H_{10}Cl_2$. Calculated %: Cl 35.32.

SUMMARY

The styrenes with three and four substituents in the nucleus: 2-chloro-3,4-dimethylstyrene, 2-chloro-3,5-dimethylstyrene, 4-chloro-2,5-dimethylstyrene and 2,3-dichloro-4,5-dimethylstyrene, which have not been described in the literature, were synthesized and characterized.

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PREPARATION OF BUTADIENE BY CATALYTIC DEHYDROGENATION OF BUTANE-BUTYLENE MIXTURES IN THE PRESENCE OF WATER VAPOR•

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One of the most important methods of preparing butadiene is the catalytic dehydrogenation of butylene. The starting butylene may be isolated from the cracking and pyrolysis gases of petroleum or obtained by catalytic dehydrogenation of butane. Both in this and in other cases, the butylene is obtained as a mixture with butane and its isolation in a pure form requires additional fractionation in the presence of a third component. In the industrial preparation of butadiene, the problem of using butane-butylene mixtures without preliminary separation could have great practical importance. Previously [1] we investigated the dehydrogenation of butane-butylene mixtures over a chromium catalyst at reduced pressure and demonstrated the possibility of obtaining butadiene in good yields. In a series of patents [2] is is pointed out that butadiene may be prepared under reduced pressure in one stage directly from butane or in two stages from butane-butylene mixtures. In the single stage process at 540-650° and a residual pressure of 35 mm, about 12.2% of the butane was converted in one pass [3]. In the two-stage process, the butane-butylene mixtures were dehydrogenated over the same catalyst (for the dehydrogenation of butane) in the presence of inert gases or at reduced pressure [4]. The yield of butadiene on butane passed was 13.8%.

The present work was undertaken to investigate the effect of water vapor on the dehydrogenation of butane-butylene mixtures on the catalyst for the dehydrogenation of butylene, which is accomplished in the presence of water vapor, since from the practical point of view, water vapor is the most suitable diluent. As is known, in the presence of certain catalysts at elevated temperatures, water vapor promotes the cracking of hydrocarbons.

EXPERIMENTAL

The experiments were carried out by a flow method in the apparatus described previously [5, 6]. Catalyst (4 ml) was placed in a quartz tube of 16 mm diameter. The starting butane-butylene mixtures were prepared in a gasometer over a saturated solution of sodium chloride. The butylene was obtained by dehydration of n-butyl alcohol over aluminum oxide and purified by distillation on a Davis column; the butane was obtained from a synthetic rubber factory and contained 1.0% of propane. The catalyzate gas was collected in a gasometer over a saturated solution of sodium chloride. The gas volumes were adjusted to normal conditions. The catalyzate gas was distilled on a Podbielniak apparatus [7] and analyzed. The butadiene content was determined on a Bushmarin apparatus with maleic anhydride [8]; butylene, butadiene and propylene were absorbed in 84% sulfuric acid; ethylene was absorbed in a solution of mercuric sulfate in sulfuric acid; carbon dioxide was absorbed with potassium hydroxide; the saturated hydrocarbons and hydrogen were combusted over copper oxide. The catalyzate gas from certain experiments was tested for carbon monoxide content with an ammoniacal solution of cuprous chloride. No carbon monoxide was detected in the gas.

Two series of experiments were carried out: one with an oxide catalyst, selective as regards dehydrogenation of butylene into butadiene, and the other with a chromium-aluminum catalyst for the dehydrogenation of butane into butylene [9, 10]. The effect of temperature, flow rate and component ratio in the starting mixture

•Work completed in 1949-1950.

TABLE 1

Effect of Composition of Butane-Butylene Mixture on the Butadiene Yield Over An Oxide Catalyst (mixture input rate 1000 liter/liter-cat·hour. Dilution with water vapor at a molar ratio of 1 : 7)

Comp. starting mix. (in vol. %)			Reacted (in mole %)			Yield of C_4H_6 (in mole %)			Composition of catalyzate gas (in volume %)									
C_4H_{10}	C_4H_8	C_3H_8	C_4H_{10}	C_4H_8	$C_4H_8+C_4H_{10}$	on mixture passed	on mixture reacted	on C_4H_8 passed	CO_2	H_2	CH_4	C_2H_4	C_2H_6	C_3H_6	C_3H_8	C_4H_8	C_4H_6	C_4H_{10}
Temperature 650°																		
—	100	—	—	42.1	—		74.3	31.3	7.4	36.8	3.2	0.2	1.0	1.8	0.4	17.0	31.2	1.0
34.4	65.0	0.6	9.4	50.6	35.4	24.1	67.0	38.4	6.3	35.6	2.1	0.8	3.5	2.5	0.4	13.3	17.7	17.4
47.8	51.6	0.6	6.0	56.9	32.3	19.4	60.4	37.4	8.0	33.7	1.9	0.6	3.7	2.7	0.7	11.0	12.6	25.4
47	51.9	0.6	6.4	49.5	28.8	18.5	64.2	35.7	6.7	31.6	2.2	1.0	3.4	2.2	0.7	10.7	15.3	25.1
58.0	41.4	0.6	6.5	53.8	26.2	16.9	65.4	40.8	6.4	30.0	2.0	0.6	3.2	2.0	0.5	10.3	11.5	32.7
Temperature 635°																		
—	100	—	—	35.0	—	—	75.2	26.3	6.0	31.6	1.6	0.4	2.5	0.6	0.6	15.8	39.0	1.0
34.4	65.0	0.6	3.0	44.5	30.1	22.0	74.2	33.9	5.5	27.7	1.0	0.4	2.4	0.8	0.8	14.7	23.6	21.0
47.8	51.6	0.6	8.8	40.3	25.2	19.0	75.3	36.8	4.8	28.2	1.1	0.8	2.3	1.0	0.7	12.3	20.0	28.3
47.4	51.9	0.6	5.6	48.6	27.1	19.8	70.4	38.3	6.4	27.9	1.3	0.5	3.1	1.3	0.8	12.6	17.1	28.6
58.0	41.4	0.6	5.4	52.3	24.0	17.4	72.4	42.0	5.6	24.5	1.5	0.4	2.4	1.7	0.5	11.6	14.4	36.8
Temperature 620°																		
39.4	60.0	0.6	3.0	32.9	21.1	18.1	86.2	30.2	3.6	22.9	1.0	0.3	1.4	0.3	0.5	13.0	29.2	27.7
47.4	51.4	0.6	4.4	45.0	25.6	19.8	78.2	38.5	5.3	24.3	0.5	0.3	3.2	0.5	0.4	13.3	19.1	30.3
58.0	41.4	0.6	2.1	35.0	15.4	12.7	80.6	30.7	3.9	18.5	1.0	0.3	1.5	0.3	0·6	9.7	20.6	43.4

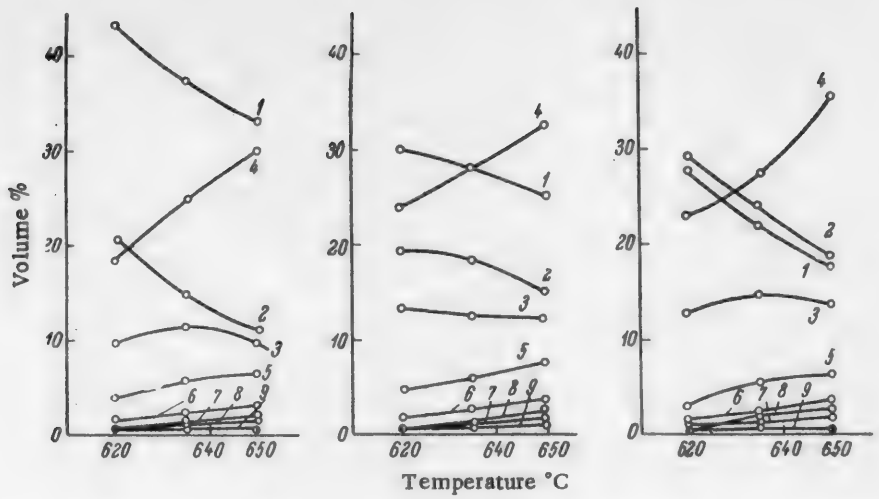


Fig. 1. Composition of catalyzate gas for three different butane-butylene mixtures over an oxide catalyst in relation to temperature. 1) C_4H_{10}, 2) C_4H_8, 3) C_4H_6, 4) H_2, 5) CO_2, 6) C_2H_6, 7) CH_4, 8) C_3H_6, 9) $C_2H_4C_3H_8$.

TABLE 2

Effect of input Rate of Butane-Butylene Mixtures on the Butadiene Yield on an Oxide Catalyst (temperature 635°; dilution with water vapor in a molar ratio of 1 : 7)

Composition of mixture (in %)		Mixture input rate (liter/liter cat · hour	Reacted (in %)			Yield of C_4H_6 (in mole %)		
C_4H_8	C_4H_{10}		C_4H_8	C_4H_{10}	mixture of C_4H_8 + C_4H_{10}	on mixture passed	on mixture reacted	on C_4H_8
51.0	49.0	14000	19.7	0.5	10.25	7.7	74.9	15.0
52.0	48.0	6800	29.5	0.9	14.8	10.2	69.2	19.7
52.0	48.0	4400	34.3	0.7	18.1	13.4	74.0	25.8
52.0	48.0	1950	40.8	3.4	22.8	15.5	68.0	30.0
51.0	49.0	1350	39.1	6.0	23.0	19.8	82.0	38.2
51.9	48.1	1000	48.6	5.6	27.1	19.8	70.4	38.3
51.6	48.4	1000	40.3	8.8	25.2	19.0	75.3	36.8

on the dehydrogenation rate of butane-butylene mixtures was investigated and experiments were carried out with pure butane and butylene. After each experiment, the catalyst was flushed with a steam – air mixture or with air.

Dehydrogenation of Butane-Butylene Mixtures Over an Oxide Catalyst. Experiments were carried out with water vapor-diluted mixtures at a molar ratio of 1 : 7 with a volume flow rate of 1000 liter/liter·cat · hour at 620, 635 and 650° with various ratios of components. The butylene content was varied from 41.4 to 65%. Experiments with pure butylene were carried out under the same conditions. The data obtained are presented in Table 1. With a decrease in the butylene content, the butadiene yields calculated on the mixture passed decreased. Thus, when the butylene content was changed from 65.0 to 41.4%, the butadiene yields fell from 24.1 to 16.9%, but calculated on the butylene passed, they increased from 38.4 to 40.8%. These yields were considerably higher than the yield of butadiene obtained in an experiment with pure butylene. As will be seen later, on this catalyst butane reacted to a small extent and the increase in the butadiene yield on the butylene in the mixture passed was apparently caused by the effect of additional dilution with butane. When the temperature was lowered from 650 to 620°, the yields of butadiene changed in the same direction, falling with a decrease in the butylene con-

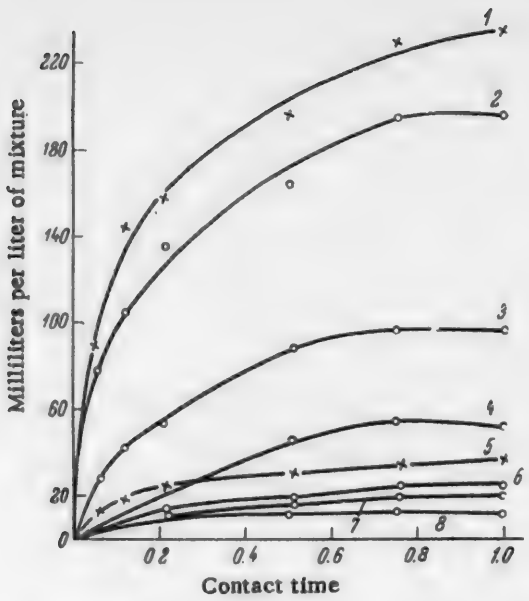


Fig. 2. Composition of catalyzate gas (in ml) in relation to the flow rate of the butane-butylene mixture at 635° on an oxide catalyst. 1) C_4H_8 (decomp.), 2) C_4H_6, 3) CO_2, 4) C_2H_6, 5) C_4H_{10}, 6) CH_4, 7) C_3H_6, 8) C_2H_4.

TABLE 3

Dehydrogenation of Butane and Butylene Over Chromium – Aluminum Catalyst With Water Vapor Dilution

Hydrocarbon	Temperature	Degree of dilution with water vapor	Increase in vol. (in %)	Composition of catalyzate gas (in vol. %)					
				C_4H_6	C_4H_8	C_2H_4	CO_2	H_2	saturated hydrocarbons
Butane	575°	1 : 5	4.5	0.3	2.0	—	1.6	—	96.1
	575	without dilution	52.0	0.8	26.0	0.4	0.6	32.2	36.6
	625	1 : 6	20.0	0.7	5.9	5.6	1.4	5.0	80.6
	650	1 : 5.6	41.0	0.5	6.9	9.8	2.8	11.0	69.0
Butylene	575	1 : 3.6	29.5	3.1	65.0	—	4.0	19.0	7.8
	600	1 : 4.9	87.6	3.5	42.7	0.4	7.4	32.8	12.0
	650	1 : 5.6	150.0	4.4	25.8	0.4	9.6	43.3	16.8

tent of the mixture, when calculated on the mixture passed, and increasing when calculated on the butylene passed. At 635° the yields of butadiene fell from 22 to 17.4% and increased, when calculated on the butylene passed, from 33.9 to 42.0%. With a decrease in temperature from 650 to 620°, the yields of butadiene calculated on the mixture reacted increased and did not depend on the composition of the mixture passed. Thus, the average yield of butadiene, calculated on the mixture reacted, was 65% at 650°, 75% at 635° and 80-82% at 620°. The change in gas composition for three different butane-butadiene mixtures in relation to temperature is shown in Fig. 1. The gas contained CH_4, C_2H_6 and C_3H_6 (2-3.5%), C_2H_4 and C_3H_8 (0.2-1.0%) and CO_2 (4-6%) and in experiments at 650° (7-8%). The amount of carbon dioxide formed, calculated on the mixture passed, was from 1.0 to 3.5% and it was largely formed as a result of the interaction of carbonaceous deposits on the surface of the catalyst with water vapor, making it possible to continue the process for a long period without regenerating the catalyst.

TABLE 4

Dehydrogenation of Butane and Butylene Over a Chromium-Aluminum Catalyst in the Absence of Diluent

	Experiment number		
	1	2	3
Starting hydrocarbon	Butane	Butylene	Temperature
Tempefature	575°	635°	635°
Input rate liter/liter cat·hour	600	2360	4290
Composition of catalyzate gas (in volume %)			
hydrogen	34.1	24.3	15.4
methane	2.2	7.7	7.4
ethylene	1.0	1.7	1.4
ethane	3.2	1.5	1.4
propylene	1.0	3.1	3.0
propane	1.4	0.2	0.4
butadiene	2.3	10.5	10.8
butylene	23.1	47.0	58.0
butane	30.0	0.7	1.4
higher hydrocarbons	0.4	2.8	1.1
Yield of butadiene on hydrocarbon passed (in %)	3.7	13.3	13.1
Yield of reaction products on hydrocarbon reacted (in mole %)			
methane	1.8	6.4	7.4
ethylene	1.6	2.8	2.9
ethane	5.1	2.9	2.4
propylene	2.4	7.4	9.3
propane	2.5	0.4	0.8
butadiene	7.3	33.1	44.5
butylene	74.0	—	—
butane	—	2.2	5.4
higher hydrocarbons	1.2	10.1	5.8
carbon on catalyst	4.0	34.6	20.4
Degree of decomposition of starting hydrocarbon (in %)	51.0	40.3	29.5

TABLE 5

Effect of Temperature and Flow Rate on the Dehydrogenation of Butane-Butylene Mixtures Over a Chromium-Aluminum Catalyst

Temperature	Mixture input rate (liter/liter cat·hour)	Composition starting mixture (in %)			Reacted (in %)			Yield of C_4H_8 (in mole %)	
		C_4H_{10}	C_4H_8	C_3H_8	C_4H_{10}	C_4H_8	$C_4H_8+C_4H_{10}$	on mixture passed	on mixture reacted
635°	2360	76.2	23.0	0.8	33.2	12.8	28.4	8.3	29.2
635	2360	52.2	47.2	0.6	31.2	29.6	30.4	11.3	37.2
635	2360	37.9	61.7	0.4	20.9	41.6	33.6	11.6	34.3
635	3350	49.0	50.4	0.6	18.5	26.4	22.1	11.6	49.5
635	2840	49.0	50.4	0.6	21.7	24.6	23.1	11.4	49.9
600	976	51.4	48.0	0.6	22.2	18.9	20.6	10.2	44.7
620	976	51.4	48.0	0.6	30.1	30.4	30.2	10.0	33.3

The effect of the flow rate was studied at 650°, with water vapor dilution in a molar ratio of 1 : 7 and at a butane-butylene ratio of 1 : 1. The flow rate of the mixture was varied from 100 to 1400 liter/liter cat·hr. The data obtained are presented in Table 2. At a flow rate of 1000-1350 liter/liter cat·hour, the yields of

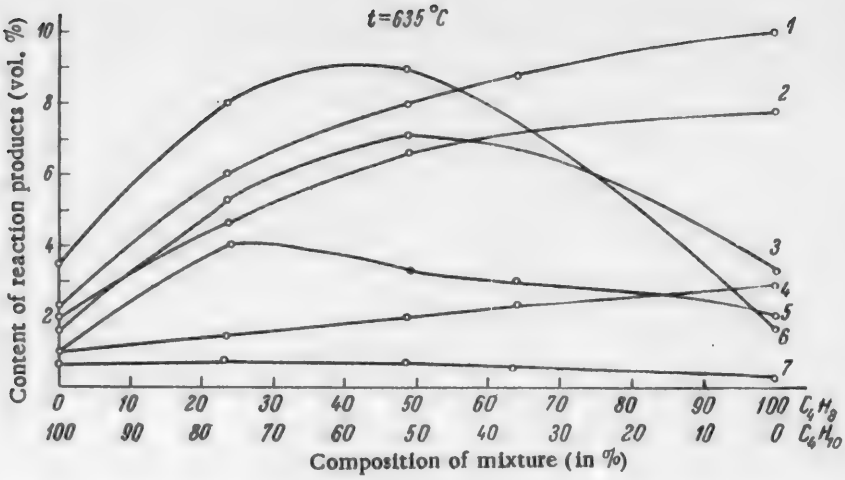


Fig. 3. Composition of reaction products in relation to ratio of butane and butylene at 635° over chromium-aluminum catalyst. 1) C_4H_6, 2) CH_4, 3) C_3H_6, 4) higher hydrocarbons, 5) C_2H_4, 6) C_2H_6, 7) C_3H_8.

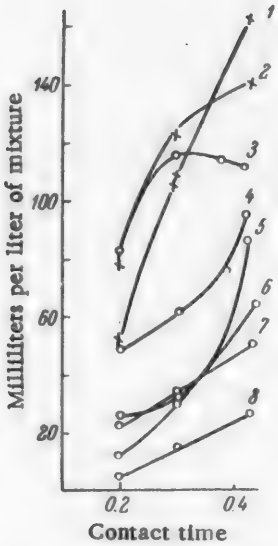


Fig. 4. Composition of catalyzate gas in relation to the flow rate of the butane-butylene mixture at 635° over a chromium-aluminum catalyst. 1) C_4H_{10}, 2) C_4H_8 (decomp.), 3) C_4H_6, 4) CH_4, 5) C_3H_6, 6) C_2H_6, 7) C_2H_4, 8) higher hydrocarbons.

butadiene were 19.8% calculated on the butane-butylene mixture passed and 38.3% on the butylene passed; the yield of butadiene calculated on the mixture reacted was 75-80%. With an increase in the flow rate of the mixture the yields of butadiene calculated on the mixture passed gradually fell and at a rate of 6800 liter/liter·cat·hour they were 10.2% and at a rate of 14000 liter/liter·cat·hour, 7.7%. The degree of conversion of the mixture fell from 27-23% to 14.8-10.2%. The change in the gas composition in relation to mixture flow rate is illustrated in Fig. 2.

Dehydrogenation of Butane Over an Oxide Catalyst. Experiments with pure butane were carried out under the same conditions: the temperature was 635°, the flow rate 1000 liter/liter·cat·hour and dilution was with water vapor in a ratio of 1 : 9. The degree of conversion of butane remained almost the same as in experiments with mixtures: about 6.7% of the butane reacted in a pass and of this about half was converted into butylene and butadiene and half was consumed in the formation of decomposition products, volatile hydrocarbons (CH_4, C_2H_4, C_2H_6) and possibly carbon on the catalyst. The formation of liquid products was not observed. The yield of butadiene calculated on the butane passed was 2% and on the butane decomposed, 29.4%.

The data obtained lead to the conclusion that water vapor is not an aggressive diluent with respect to butane on the catalyst investigated and that the main direction of the reaction is the dehydrogenation of butane into butylene and butadiene, which is accompanied by the formation of a small amount of volatile hydrocarbons as a result of cracking at high temperature.

Dehydrogenation of Butane and Butadiene Over Chromium-Aluminum Catalyst With Water Vapor Dilution. Experiments were carried out over the temperature range 575-650° with a flow rate of 1000 liter/liter·cat·hour and dilution with water vapor in a molar ratio of 1 : 5-6. The data obtained are presented in Table 3. Water vapor strongly inhibited the dehydrogenation of butane into butylene over this catalyst. When butylene

was passed in the presence of water vapor a considerable conversion of butylene was observed with the formation of decomposition products and the butadiene content of the gas did not exceed 3.1-4.4%. The results of experiments showed that water vapor was quite unsuitable as a diluent in work with a chromium-aluminum catalyst.*

Dehydrogenation of Butane and Butylene Over a Chromium-Aluminum Catalyst Without Diluent. Experiments with butane without diluent were carried out at 575° and a flow rate of 600 liter/liter·cat·hour. The experiments with butylene were at 635° and to reduce the decomposition of butylene and the dehydrogenation product, butadiene, the butylene was passed at higher rates (2360 and 4290 liter/liter·cat·hour). Balance experiments were carried out under these conditions. The results of the experiments are presented in Table 4. The butadiene yields, calculated on butane reacted were 74.0% at a total butane conversion of 51%. In addition, there were formed light hydrocarbons, butadiene (7.1%), condensation products, i.e. liquid hydrocarbons (1.2%) and carbon on the catalyst (4.0%).

The dehydrogenation of butylene under the given conditions was accompanied by considerable formation of side products from decomposition. The yield of butadiene was 13.3% calculated on the butylene passed and 33.1% on that decomposed at a flow rate of 2360 liter/liter·cat·hour. With an increase in the flow rate to 4290 liter/liter·cat·hour, the butadiene yield calculated on the butylene decomposed increased to 44.5% with a fall in the total conversion of butylene from 40.3 to 29.5%. The side products of the reaction were light hydrocarbons and condensation and polymerization products and a considerable amount of carbon was deposited on the catalyst, representing 34.6% at a rate of 2360 liter/liter·cat·hour and 20.4% at a rate of 4290 liter/liter·cat·hour, calculated on the butylene decomposed (Table 4). Thus, the chromium-aluminum catalyst was not selective in the dehydrogenation of butylene and promoted the decomposition of butylene and the formation of butadiene as is indicated by the character of the reaction products.

Dehydrogenation of Butane-Butylene Mixtures Over Chromium-Aluminum Catalyst. The experiments were carried out at lhigh mixture flow rates as in the experiments with pure butylene. Using differnet ratios of components in the mixture, experiments were carried out at 635° and a flow rate of 2360 liter/liter·cat·hour. Variation of the component ratio in the mixture had little effect on the butadiene yields, which were from 8.3 to 11.6%, calculated on the mixture passed, and did not exceed 37.2% on that reacted. The composition of the catalyzate gas with a variation in the ratio of the components is illustrated in Fig. 3. At the same temperature and at a component ratio of 1 : 1, increasing the flow rate to 3350 liter/liter·cat·hour increased the yields of butadiene calculated on the mixture reacted to 49.5% with the same yield on the mixture passed (11.6%). With an increase in the flow rate, the degree of decomposition fell from 30.4 to 22.4%. Similar results were obtained in experiments at 600 and 620° with a flow rate of 980 liter/liter·cat·hour (the butadiene yields were 10% on the mixture passed and 33-44% on that reacted). The data obtained are presented in Table 5, which gives the compositions of the products. The change in composition of the reaction products in relation to contact time is shown in Fig. 4. The optimal contact time lay close to 0.3 sec. With a longer contact time the degree of decomposition of the mixture and the formation of light hydrocarbons increased and with a shorter contact time, there was less reaction of the mixture.

From a comparison of the data obtained on the two catalysts it follows that the dehydrogenation of butane-butylene mixtures over an oxide catalyst proceeds with higher yields of butadiene calculated both on the mixture passed and on the mixture reacting at a higher degree of mixture conversion in a pass than in the case of the chromium-aluminum catalyst. Dehydrogenation proceeded in the presence of water vapor, which considerably facilitated the process in comparison with inert diluents or the use of reduced pressure and made it possible to carry out the process in long cycles without regenerating the catalyst. The results obtained are of interest also in that they offer the possibility of partially reducing the energy consuming stage of separating butane-butylene mixtures in the general scheme for preparing butadiene from butane and from cracking gases.

SUMMARY

1. The dehydrogenation of butane-butylene mixtures may be carried out in the presence of water vapor on an oxide catalyst for the dehydrogenation of butylene. At 620-635°, a flow rate of 1000-1350 liter/liter·cat·hour and dilution with water vapor in a molar ratio of 1 : 7-8, the yields of butadiene were 19.8% calculated on the mixture passed, about 40% on the butylene passed and 75-80% on the mixture reacted.

The process may be carried out in long cycles without regeneration of the catalyst.

*The chromium-aluminum catalyst was presented to us by M. N. Marushkin.

2. Over a chromium-aluminum catalyst, water vapor hindered the dehydrogenation of butane into butylene and promoted conversions of butylene with the formation of decomposition products. In the dehydrogenation of butane-butylene mixtures over a chromium-aluminum catalyst in the absence of diluent at 635°, a flow rate of 2360-3350 liter/liter-cat · hour and a component ratio of 1 : 1, the yields of butadiene were 11.6% calculated on the mixture passed and 37-49.5% on that decomposed. The catalyst was rapidly covered with carbon and required frequent regeneration.

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CATALYTIC CONVERSIONS OF 1,1-DIMETHYLCYCLOHEXANE AND 1-METHYL-1-ETHYLCYCLOHEXANE IN THE PRESENCE OF AN ALUMINOSILICATE CATALYST

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Cycloparaffins containing a quaternary carbon atom in a six-membered ring are found in petroleum. Thus, investigations of the individual composition of benzines from petroleum from various deposits showed that benzines from Surakhan, Embin, Tuimazin and Karachukur oils contained 1,1-dimethylcyclohexane and 1,1,3-trimethylcyclohexane [1]. Work has also been done [2] on the conversions of 1,1-dimethylcyclohexane on an aluminosilicate catalyst at 540°. Due to the fact that the authors of this had small amounts of hydrocarbon for the investigation, they did not carry out a detailed analysis of the gaseous and liquid portions of the catalyzate. It therefore seemed interesting to study the behavior of the simplest gem-methylalkylcyclohexanes under catalytic cracking conditions on an aluminosilicate catalyst. For this purpose we studied the behavior of 1,1-dimethylcyclohexane and 1-methyl-1-ethylcyclohexane on an aluminosilicate catalyst at 500°. We thus obtained gaseous products, a liquid condensate and coke deposited on the catalyst.

The gaseous products obtained were first subjected to low-temperature fractionation and the composition of the fractions obtained was then investigated on a VTI (All-Union Heat Engineering Institute) apparatus. To establish the composition of the liquid catalyzate we used sharp fractionation, chromatographic adsorption on silica gel and optical and chemical investigation methods.

On the basis of the analysis we established the following approximate weight percent composition of the conversion products of 1,1-dimethylcyclohexane: gaseous hydrocarbons 21.4, liquid paraffinic hydrocarbons 2.6, naphthene hydrocarbons 8.4, aromatic hydrocarbons 45.2 and coke 22.4.

For 1-methyl-1-ethylcyclohexane we found the following composition (in weight %): gaseous hydrocarbons 10.8, mixture of paraffinic and naphthene hydrocarbons 23.0, aromatic hydrocarbons 40.5 and coke 25.7.

From a consideration of the experimental data we can assume that on an aluminosilicate catalyst there occurs successive or simultaneous removal of one or two alkyl groups from the gem-dialkylcyclohexane with partial isomerization of the ring and hydrogenation due to disproportionation of hydrogen. There is also dehydrogenation of the cyclohexane and methylcyclohexane formed to benzene and toluene. A considerable portion of the six-membered naphthenes are methylated by the cracking products with the formation of mainly di- and trimethylsubstituted cyclohexanes with their subsequent dehydrogenation to the corresponding aromatic hydrocarbons. Also we cannot exclude the possible formation of substituted aromatic hydrocarbons due to methylation of the benzene ring. The process of aromatic hydrocarbon formation is apparently complicated by the disproportionation of methyl groups under the catalysis conditions chosen [3-5]. The paraffinic hydrocarbons contained in the catalyzates are apparently the cracking products of naphthenes.

The direction of the catalytic conversions of gem-dialkylcyclohexanes are illustrated by the scheme (see page 2184).

TABLE 1

Components	Composition of gas (in %)	
	volume	weight
Hydrogen	42.1	4.5
Methane	31.5	27.0
Ethylene	1.2	1.7
Ethane	1.1	1.7
Propane	14.5	33.9
Isobutylene	0.1	0.1
Butane (mixture)	9.5	31.1
ΣC_nH_{2n}	1.3	1.8
ΣC_nH_{2n+2}	98.7	98.2
$\Sigma C_nH_{2n}/\Sigma C_nH_{2n+2}$	0.013	0.018

TABLE 2

Fraction No.	Boiling range at 737 mm	n_D^{20}	d_4^{20}	Amount of products	
				in g	in weight %
1	30.0— 82.6°	1.3940	0.6733	0.50	1.0
2	82.6—110.2	1.4390	0.7714	1.77	3.5
3	110.2—114.0	1.4421	0.7927	1.14	2.3
4	114.0—117.1	1.4342	0.7878	1.35	2.7
5	117.1—120.0	1.4290	0.7770	34.57	68.9
6	120.0—126.0	1.4380	0.8150	1.24	2.5
7	126.0—139.4	1.4861	0.8544	3.98	7.9
8	139.4—152.0	1.5002	0.8542	1.35	2.7
	Residue	1.5235	0.9081	2.50	5.0
	Losses	—	—	1.80	3.5

EXPERIMENTAL

Synthesis of Starting Hydrocarbons*

1,1-Dimethylcyclohexane [6, 7]. By reduction with amalgamated aluminum in dry benzene, from cyclopentanone and acetone we obtained 1-isopropylcyclopentane-1,6-diol. By the action of 63% sulfuric acid on the mixed pinacone, the latter was converted into 1,1-dimethylcyclohexanone-2. The hydrazone obtained was reduced in diethylene glycol in the presence of solid potassium hydroxide to give 1,1-dimethylcyclohexane in 72.3% yield. After chromatography and distillation on an 80 theoretical plate column, the 1,1-dimethylcyclohexane had the following constants:

B.p. 118.8-118.9° (750 mm), $n^{20}D$ 1.4297, d_4^{20} 0.7765, MR_D 37.23. C_8H_{16}. Calculated 36.94.

Literature data [6]: b.p. 119.2-119.4° (748 mm), $n^{20}D$ 1.4296, d_4^{20} 0.7803.

1-Methyl-1-ethylcyclohexane [8]. We synthesized 1-methylcyclohexanol-1 from cyclohexanone and methylmagnesium bromide. 1-Chloro-1-methylcyclohexane was prepared by shaking the tertiary alcohol with hydrochloric acid. Reaction of the chloro compound with diethylzinc in tetralin yielded 1-methyl-1-ethylcyclohexane in 37% yield.

After chromatography and fractionation on an 80 theoretical plate column, the 1-methyl-1-ethylcyclohexane obtained had the following properties:

B.p. 151.0-151.2° (744.5 mm), $n^{20}D$ 1.4420, d_4^{20} 0.8050, MR_D 41.42. C_9H_{18}. Calculated 41.56.

Literature data [9]: b.p. 151.6-151.8° (748 mm), $n^{20}D$ 1.4422, d_4^{20} 0.8053.

* See scheme on p. 2184.

TABLE 3

Catalysis products	Amount of products	
	in g	in weight %
Gaseous hydrocarbons	4.1	21.4
Liquid paraffinic hydrocarbons	0.5	2.6
Naphthene hydrocarbons:	1.6	8.4
Cis-1,2-dimethylcyclopentane	1.0	5.3
Methylcyclohexane	0.6	3.1
Aromatic hydrocarbons:	8.7	45.2
Toluene	1.1	5.7
p-Xylene	1.6	8.3
m-Xylene	2.9	15.1
o-Xylene	1.1	5.7
1,3,5-Trimethylbenzene	0.5	2.6
1,2,4-Trimethylbenzene	1.5	7.8
Coke	4.3	22.4
Total	19.2	100

TABLE 4

Components	Composition of gas (in %)	
	volume	weight
Hydrogen	16.1	0.7
Methane	9.6	3.9
Ethylene	0.8	0.5
Ethane	7.2	5.7
Propylene	0.8	1.0
Propane	29.0	33.2
n-Butylene	1.3	2.0
Butanes (mixture)	35.2	53.0
ΣC_nH_{2n}	2.9	3.5
ΣC_nH_{2n+2}	81.0	95.8
$\Sigma C_nH_{2n}/\Sigma C_nH_{2n+2}$	0.036	0.036

Catalytic Conversions of Hydrocarbons

The catalytic conversions of the hydrocarbons were studied on a flow system apparatus with automatic input of the hydrocarbon. The temperature was controlled with a chromel-alumel thermocouple, which was placed in a glass pocket in the reaction tube, running through into the catalyst bed. Before an experiment, the whole system was flushed with nitrogen. After each hour of operation, the catalyst was regenerated in a stream of dry air at 500-550° for 5-6 hours. The coke content was determined from the amount of carbon dioxide liberated, which was absorbed on ascarite.

Catalytic Conversions of 1,1-Dimethylcyclohexane. In preliminary experiments we determined the effect of temperature on degree of conversion of gem-dialkylcyclohexanes on the example of 1,1-dimethylcyclohexane. It was thus established that considerable conversion of the hydrocarbon (the degree of conversion was 42.4%) was observed at 500°; the latter was taken as the optimal temperature for the conversion of gem-dialkylcyclohexanes.

1,1-Dimethylcyclohexane was passed at a rate of 13.95 ml/hour (volume rate 0.23 liter/liter/hour) over aluminosilicate catalyst (33.7 g), placed in a uniformly heated part of the reaction tube, after the catalyst had been dried and its activity stabilized at 500°. To obtain a sufficient amount of catalyzate for the investigation, we carried out 6 experiments, as a result of which 65.28 g (0.58 mole) of the hydrocarbon investigated was passed over the catalyst and we obtained 52.0 g of liquid catalyzate with $n^{20}D$ 1.4398, 4900 ml (4.1 g) of gas and 4.32 g of coke.

TABLE 5

Fraction No.	Boiling range at 752 mm	n_D^{20}	d_4^{20}	Amount of products	
				in g	in weight %
1	41.0— 78.5°	1.3840	0.6843	0.4	1.7
2	78.5—115.0	1.4172	0.7560	1.4	5.8
3	115.0—136.0	1.4510	0.8014	0.72	3.0
4	136.0—149.3	1.4630	0.8372	1.64	6.8
5	149.3—153.0	1.4422	0.8056	15.93	65.9
6	153.0—169.0	1.4890	0.8567	0.56	2.3
	Residue .	1.5122	—	2.00	8.3
	Losses . .	—	—	1.50	6.2
	Total . .	--	—	24.15	100

TABLE 6

Catalysis products	Amount of products			
	in g		in weight %	
Gaseous hydrocarbons	0.8		10.8	
Mixture of paraffinic and naphthene hydrocarbons	1.7		23.0	
Aromatic hydrocarbons: .	3.0		40.5	
Benzene		0.1		1.3
Toluene		0.2		2.7
p-Xylene		0.4		5.4
m-Xylene		0.8		10.8
1,3,5-Trimethylbenzene		1.5		20.3
1,2,4-Trimethylbenzene				
Coke	1.9		25.7	
Total	7.4		100	

The gaseous catalysis products were subjected to low-temperature distillation on a TsIATIM-51-V apparatus (TsIATIM = Central Sci. Res. Inst. of Aviation Fuels and Lubricants) Then the fractions were analyzed on a VTI apparatus. The results of the analysis are presented in Table 1.

The catalyzate obtained was fractionated on a column with an efficiency of 80 theoretical plates. The results of the distillation are shown in Table 2.

The 1st fraction contained mainly paraffinic hydrocarbons.

The 2nd and 3rd fractions were combined and investigated optically. Plotting the Raman spectrum gave the following approximate composition (in %): cis-1,2-dimethylcyclopentane 34, methylcyclohexane 21, toluene 35 and 1,1-dimethylcyclohexane 10.

To identify the toluene from the fraction investigated, we prepared the dinitro derivative with m.p. 69-70° (after two recrystallizations from ethanol); a mixed melting point with authentic 2,4-dinitrotoluene was not depressed.

The 4th and 6th fractions, judging by the refractive index, contained mainly 1,1-dimethylcyclohexane with toluene in the 4th fraction and with xylenes in the 6th fraction (toluene and xylenes, respectively, were detected in the 3rd and 7th fractions). Calculation from the refractive index gave the following approximate composition for the 4th fraction (in %): toluene 13, and 1,1-dimethylcyclohexane 87; for the 6th fraction (in %): toluene 13 and 1,1-dimethylcyclohexane 87%.

The 5th fraction, judging by its properties, was the original 1,1-dimethylcyclohexane.

The 7th and 8th fractions were combined and investigated optically. A study of the Raman spectra showed that the combined fraction had the following percent composition: p-xylene 30, m-xylene 50 and o-xylene 20%.

For qualitative confirmation of the composition of the aromatic hydrocarbons, the latter were oxidized with potassium permanganate [10]. Oxidation of 1.5 ml of fraction yielded 2.9 g of crude, solid carboxylic acids. As a results of successive separation of the acids we isolated 0.1 g of o-phthalic acid (positive reaction with resorcinol), which melted at 189-190° in a sealed capillary; the anhydride of the acid, obtained by sublimation on heating the acid to 240°, had m.p. 130°, 0.26 g of isophthalic acid and 0.17 g of terephthalic acid.* The methyl esters were obtained from the latter. The dimethyl ester of isophthalic acid melted at 66-67° and the dimethyl ester of terephthalic acid at 139-140°.

The residue boiled in the range 158-175° ($n^{20}D$ 1.5061) and according to the Raman spectrum data was a mixture of 1,3,5-trimethylbenzene (25%) and 1,2,4-trimethylbenzene (75%).

On the basis of the investigations, we calculated the approximate percent composition of the products obtained as a result of catalytic conversions of 1,1-dimethylcyclohexane on an aluminosilicate catalyst at 500° (allowing for the amount of unchanged starting hydrocarbon) and this is presented in Table 3.

The degree of hydrocarbon conversion was 42.4% (calculated on the amount of starting hydrocarbon subjected to catalysis).

Catalytic Conversions of 1-Methyl-1-ethylcyclohexane. 1-Methyl-1-ethylcyclohexane was studied under the same conditions as 1,1-dimethylcyclohexane, i.e., at 500° and a volume rate of 0.23 liter/liter/hour. 37.43 g (0.3 mole) of hydrocarbon was passed over the catalyst and we obtained 30.98 g of liquid catalyzate with $n^{20}D$ 1.4548, 600 ml (1.05 g) of gas and 2.43 g of coke.

After fractionation on a TsIATIM-52 apparatus, the gaseous catalysis products were investigated on a VTI apparatus. The composition of the gas obtained is presented in Table 4.

The fractions isolated from the liquid catalyzate by fractionation on an 80 theoretical plate column and their properties are presented in Table 5.

The 1st fraction, judging by the constants, consisted mainly of a mixture of paraffinic hydrocarbons.

The 2nd fraction contained about 3% of benzene and 7% of toluene according to the ultraviolet absorption spectrum. Due to the small amount, the nonaromatic part was not investigated. However, the absence of unsaturated hydrocarbons from this fraction and the constants of the fraction indicate that it was mainly a mixture of paraffinic and naphthene hydrocarbons.

The 3rd and 4th fractions were combined and subjected to chromatographic adsorption on silica gel. The constants of the dearomatized part (1.45 g was isolated) [b.p. 148.5-150.0° (739 mm), $n^{20}D$ 1.4419, d_4^{20} 0.8053], indicate that it consisted of the starting hydrocarbon. The aromatic part of the fraction (0.55 g) had the following constants: b.p. 135-142° (756 mm) (according to Sivolobov's method), $n^{20}D$ 1.4966, d_4^{20} 0.8651 and was examined on an IKS-11 infrared spectrometer. The fraction was found to contain 40% of p-xylene and 60% of m-xylene by the procedure of Young et al. [11].

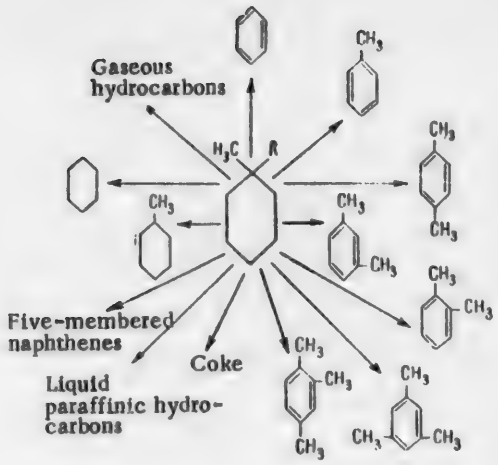
The 5th fraction, judging by its properties, was unchanged 1-methyl-1-ethylcyclohexane. The Raman spectrum confirmed this.

The 6th fraction was studied by infrared spectroscopy [11]. It was found that the fraction consisted of a mixture of 70% of 1,3,5-trimethylbenzene and 30% of 1,2,4-trimethylbenzene.

The residue obtained on fractionating the catalyzate and boiling over the range 170.0-180.0° and having $n^{20}D$ 1.5108 was studied by an optical method. According to the Raman spectrum, the residue contained 1,3,5-trimethylbenzene (~25%) and 1,2,4-trimethylbenzene (~75%).

On the basis of the above investigations we present the following approximate percent composition for the catalysis products, calculated on the amount of 1-methyl-1-ethylcyclohexane changed on passing over the catalyst at 500° (Table 6). The degree of conversion of the hydrocarbon was 42.5%.

*As in original-Publisher's note.



SUMMARY

1. A study was made of the conversions of 1,1-dimethylcyclohexane and 1-methyl-1-ethylcyclohexane in contact with aluminosilicate catalyst at 500°.

2. Under the catalysis conditions chosen, processes occurred with the elimination of alkyl groups from the quaternary carbon atom in the ring, hydrocracking, methylation and aromatization, and there was also isomerization of six-membered rings into five-membered ones. It was established that the main conversion products were aromatic hydrocarbons, while paraffinic and napthene hydrocarbons were formed to a lesser extent.

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CATALYTIC CONVERSIONS OF 1-METHYL-1-PROPYLCYCLOHEXANE AND 1-METHYL-1-BUTYLCYCLOHEXANE ON AN ALUMINOSILICATE CATALYST

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Continuing investigations of the behavior of gem-dialkylcyclohexanes under catalytic cracking conditions [1], we synthesized 1-methyl-1-propylcyclohexane and 1-methyl-1-butylcyclohexane and studied their conversions on an aluminosilicate catalyst at 500°.

Under the chosen catalysis conditions, the hydrocarbons yielded gaseous hydrocarbons, a liquid condensate and coke deposited on the catalyst. The gaseous products were subjected to low-temperature fractionation on a TsIATIM-51-U apparatus (TsIATIM = Central Sci. Res. Inst. of Aviation Fuels and Lubricants), following which the fractions isolated were investigated on a VTI (All-Union Heat Engineering Institute) apparatus. To establish the composition of the liquid part of the catalyzate we used sharp fractionation, chromatographic adsorption on silica gel and optical and chemical investigation methods.

As a result of analyzing the conversion products of 1-methyl-1-propylcyclohexane, we obtained the following composition (in weight %): gaseous hydrocarbons 23.8, liquid paraffinic hydrocarbons 5.9, naphthene hydrocarbons 20.5, aromatic hydrocarbons 33.3 and coke 16.5. From 1-methyl-1-butylcyclohexane we obtained (in weight %): gaseous hydrocarbons 30.6, liquid paraffinic hydrocarbons 4.8, naphthene hydrocarbons 17.0, aromatic hydrocarbons 41.8 and coke 5.8.

The results obtained largely confirmed the rules we observed on studying the catalytic conversions of 1,1-dimethylcyclohexane and 1-methyl-1-ethylcyclohexane. The main catalytic conversion products of the hydrocarbons studied were also aromatic hydrocarbons with a ratio of m-xylene to p-xylene formed of 2:1 and a ratio of liquid paraffins to naphthenes in the catalyzate of 1:3.5 regardless of the starting gem-dialkylcyclohexane.

The saturated hydrocarbons propane and butane predominated in the gaseous products. It should be noted that with an increase in the number of carbon atoms in the alkyl group of gem-methylalkylcyclohexanes, the degree of conversion during catalysis increased from 42.4% for 1,1-dimethylcyclohexane to 84.2% for 1-methyl-1-butylcyclohexane.

EXPERIMENTAL

Synthesis of 1-Methyl-1-propylcyclohexane [2]. From cyclohexanone and methylmagnesium bromide we obtained 1-methylcyclohexanol-1. By shaking with hydrochloric acid, the tertiary alcohol obtained was converted into 1-chloro-1-methylcyclohexane. An ether solution of the chloride, mixed with 5 g of mercuric chloride was slowly added to an ether solution of propylmagnesium bromide. The reaction mixture was heated for 50 hours then the bulk of the ether was removed and 400 ml of dry toluene added, after which the contents of the reaction flask were heated at the boiling point of toluene for a further 10 hours. After decomposition of the reaction mixture, the ether and toluene were removed and the residue boiled over sodium and fractionated

TABLE 1

Components	Composition of gas (in %)	
	volume	weight
Hydrogen	15.4	0.8
Methane	10.9	4.4
Ethylene	4.5	3.0
Ethane	2.7	2.1
Propylene	2.9	3.1
Propane	27.0	30.1
Isobutylene	0.2	0.3
n-Butylene	0.2	0.4
Butanes (mixture)	36.2	55.8
ΣC_nH_{2n}	7.8	6.8
ΣC_nH_{2n+2}	76.8	76.8
$\Sigma C_nH_{2n}/\Sigma C_nH_{2n+2}$	0.101	0.073

TABLE 2

Fraction No.	Boiling range at 749 mm	n_D^{20}	d_4^{20}	Amount of products	
				g	%
1	31.5— 71.5°	1.3823	0.6817	4.32	4.2
2	71.5— 73.0	1.4122	0.7484	1.61	1.5
3	73.0—108.0	1.4257	0.7638	11.39	11.0
4	108.0—109.5	1.4959	0.8660	4.05	4.0
5	109.5—136.0	1.4960	0.8673	0.30	0.3
6	136.0—147.0	1.4983	0.8730	5.46	5.3
7	147.0—169.0	1.4842	0.8594	0.2	0.2
8	169.0—172.0	1.4450	0.8081	68.29	66.0
	Residue	1.5257	—	6.41	6.2
	Losses	—	—	1.35	1.30

to give a 12.6% yield of 1-methyl-1-propylcyclohexane. After chromatography and distillation on an 80 theoretical plate column, the hydrocarbon had the following properties:

B.p. 172.3-172.5° (749 mm), 67.0-67.2° (22 mm), $n^{20}D$ 1.4459, d_4^{20} 0.8076, MR_D 46.18; calc. 46.18.

Literature data [2]: b.p. 172.5-172.8° (756 mm), 67.0-67.5° (22 mm), $n^{20}D$ 1.4445, d_4^{20} 0.8077.

Synthesis of 1-Methyl-1-butylcyclohexane [3]. By the method described above we synthesized 1-methyl-1-butylcyclohexane in 6% yield from butylmagnesium bromide and 1-chloro-1-methylcyclohexane by the Grignard – Wurtz reaction. After chromatography and distillation on an 80 theoretical plate column, the hydrocarbon had the constants:

B.p. 191.5-192.0° (756 mm), 73.0-73.2° (12 mm), $n^{20}D$ 1.4480, d_4^{20} 0.8138, MR_D 50.66. $C_{11}H_{22}$. Calculated 50.80.

Literature data [3]: b.p. 191.5° (758 mm), $n^{20}D$ 1.4477, d_4^{20} 0.8133.

Catalytic Conversions of Hydrocarbons

The hydrocarbon was fed into a flow-type apparatus automatically at a volume rate of 0.23 liter/liter/hour. The experiments were carried out at 500°. After each hour of operation, the catalyst was regenerated for 5-6 hours in a stream of dry air at 500-550°. The carbon dioxide liberated thus was absorbed with ascarite and from the increase in weight of the latter we determined the amount of coke deposited on the catalyst.

Before a catalysis experiment, the system was flushed with nitrogen and the experiments were carried out without a carrier gas.

TABLE 3

Catalysis products	Amount of products	
	g	%
Gaseous hydrocarbons	13.3	23.8
Liquid paraffinic hydrocarbons	3.3	5.9
Isopentane	2.0	3.6
2-Methylpentane	1.3	2.3
Naphthene hydrocarbons	11.4	20.5
Cyclopentane	0.9	1.6
Methylcyclopentane	1.6	2.9
Cyclohexane	1.5	2.7
Methylcyclohexane	7.4	13.3
Aromatic hydrocarbons	18.6	33.3
Benzene	0.2	0.3
Toluene	6.8	12.2
m-Xylene	1.6	2.9
p-Xylene	3.0	5.4
o-Xylene	1.0	1.8
1,3,5-Trimethylbenzene	1.5	2.7
1,2,4-Trimethylbenzene	4.5	8.0
Coke	9.2	16.5

TABLE 4

Components	Composition of gas (in %)	
	volume	weight
Hydrogen	20.5	1.2
Methane	15.4	7.1
Ethylene	1.5	1.1
Ethane	7.5	6.6
Propylene	5.5	6.3
Propane	18.1	22.9
n-Butylene	6.4	12.1
Butanes (mixture)	25.1	42.7
ΣC_nH_{2n}	13.4	19.5
ΣC_nH_{2n+2}	66.1	79.3
$\Sigma C_nH_{2n}/\Sigma C_nH_{2n+2}$	0.155	0.242

Catalytic Conversion of 1-Methyl-1-propylcyclohexane. Under the catalysis conditions chosen, 147.29 g (1.1 mole) of methyl-1-propylcyclohexane was passed over an aluminosilicate catalyst (33.7 g); we obtained 112.3 g of liquid catalyzate with $n^{20}D$ 1.4590, 8250 ml (14.46 g) of gas and ~10.01 g of coke.

The results of the gas analysis are presented in Table 1.

Fractionation of the liquid catalyzate obtained on a column with an efficiency of 80 theoretical plates yielded the following fractions (Table 2).

The 1st fraction (b.p. 31.5-71.5°) was shown to contain the following components by means of the Raman spectrum (in %): isopentane 45, cyclopentane 20, 2-methylpentane 30 and benzene 5.

2nd fraction (b.p. 71.5-73.0°). According to its constants, this fraction corresponded to methylcyclopentane; literature data for methylcyclopentane [4]: b.p. 71.9° (760 mm), $n^{20}D$ 1.4099, d_4^{20} 0.7488. The presence of methylcyclohexane was also confirmed by plotting the infrared-absorption spectrum.

The 3rd fraction (b.p. 73.0-108.0°) had the following composition (in %) according to the Raman spectrum: cyclohexane 13, methylcyclohexane 65 and toluene 22.

TABLE 5

Fraction No.	Boiling range at 738 mm	n_D^{20}	d_4^{20}	Amount of products	
				g	%
1	30.5— 70.5°	1.3833	0.6825	1.08	3.5
2	70.5— 78.3	1.4190	0.7450	2.99	9.8
3	78.3— 98.5	1.4155	0.7482	1.17	3.8
4	98.5—108.2	1.4421	0.7865	1.90	6.2
5	108.2—113.0	1.4768	0.8371	1.50	4.9
6	113.0—120.0	1.4769	0.8385	0.59	1.9
7	120.0—150.0	1.4925	0.8808	4.13	13.5
8	150.0—175.0	1.4891	0.8794	3.17	10.4
9	175.0—185.0	1.4641	0.7857	2.12	7.0
10	67.2— 74.0 (10 mm)	1.4770	0.8138	6.93	22.7
	Residue . . .	1.5538	0.9651	3.38	11.1
	Losses	—	—	1.60	5.2

TABLE 6

Catalysis products	Amount of products	
	g	%
Gaseous hydrocarbons	9.0	30.6
Liquid paraffinic hydrocarbons	1.4	4.8
Naphthene hydrocarbons	5.0	17.0
Methylcyclopentane	2.3	7.8
Methylcyclohexane . . .	2.7	9.2
Aromatic hydrocarbons . . .	12.3	41.8
Benzene . . .	0.5	1.7
Toluene . . .	2.7	9.2
p-Xylene . . .	1.2	4.1
m-Xylene	2.5	8.5
o-Xylene	1.1	3.7
1,3,5-Trimethylbenzene	0.6	2.0
1,2,4-Trimethylbenzene	3.7	12.6
Coke	1.7	5.8

The 4th fraction corresponded to toluene in its constants. Literature data for toluene [5]: b.p. 110.5° (760 mm), $n^{20}D$ 1.4962, d_4^{20} 0.8665. The Raman spectrum confirmed this supposition. The dinitroderivative obtained from this fraction melted at 69-70°. A mixed melting point with authentic 2,4-dinitrotoluene was not depressed.

The 5th fraction was an intermediate between the 4th (toluene) and 6th (xylene) fractions. Its approximate composition, calculated from the refractive index was toluene 96% and xylene 4%.

The 6th fraction was shown to contain 30% of p-xylene, 52% of m-xylene and 18% of o-xylene on the basis of the Raman spectrum. The composition of the fraction was confirmed qualitatively by oxidizing the aromatic hydrocarbons present with potassium permanganate [6]. Oxidation of 1.8 g of fraction yielded 3.83 g of crude, solid carboxylic acids and by successive separation, this yielded (in g): orthophthalic acid 0.66, isophthalic acid 1.05 and terephthalic acid 0.80.

The orthophthalic acid isolated (positive reaction with resorcinol) melted at 190-191° and when it was heated to 240° in a sealed capillary, phthalic anhydride with m.p. 130° sublimed from it. The methyl esters were prepared from isophthalic and terephthalic acids. Methyl isophthalate melted at 66-67° and the melting point of the methyl terephthalate was 139-140°.

The 7th fraction was probably a mixture of xylenes and the starting hydrocarbon; the approximate composition of the fraction calculated from the refractive index was xylenes 74% and 1-methyl-1-propylcyclohexane 26%.

The 8th fraction was probably the starting 1-methyl-1-propylcyclohexane. The Raman spectrum confirmed this supposition.

The residue (b.p. 165.8-178.0°, $n^{20}D$ 1.5113), obtained on distilling the catalyzate on a fractionating column, contained the following according to Raman spectrum data: 1,3,5-trimethylbenzene 25% and 1,2,4-trimethylbenzene 75%.

On the basis of the data presented above, Table 3 gives the approximate percent composition of the catalysis products, calculated on the 1-methyl-1-propylcyclohexane converted.

The degree of conversion of the hydrocarbon was 49.5% (calculated on the amount of starting hydrocarbon taken).

Catalytic conversions of 1-methyl-1-butylcyclohexane were studied under the same conditions as for 1-methyl-1-propylcyclohexane. From 64.5 g (0.42 mole) of 1-methyl-1-butylcyclohexane we obtained 44.6 g of liquid catalyzate with $n^{20}D$ 1.4633, 8500 ml (13.1 g) of gas and 2.5 g of coke.

The composition of the gaseous catalysis products is presented in Table 4.

The fractions isolated by distillation of the liquid catalyzate on a column with an efficiency of 40 theoretical plates and their properties are presented in Table 5.

The 1st fraction consisted mainly of paraffinic hydrocarbons.

The 2nd-4th fractions were combined and had the following composition (in %) according to Raman spectrum data: methylcyclopentane 37, benzene 8, methylcyclohexane 35 and toluene 20.

The 5th and 6th fractions were combined and subjected to chromatographic adsorption on silica gel to separate the aromatic hydrocarbons from paraffins and naphthenes. The constants of the 0.55 g of the dearomatized part of the fraction isolated by chromatography [b.p. 99-103° (756 mm) (determined by Sivolobov's method), $n^{20}D$ 1.4232, d_4^{20} 0.7699] indicated that it contained methylcyclohexane, which was also detected in the preceding fraction of the catalyzate. Literature data for methylcyclohexane [3]: b.p. 100.3° (760 mm), $n^{20}D$ 1.4230, d_4^{20} 0.7692.

The 1.34 g of the aromatic part of the fraction obtained corresponded to toluene in its constants [5] [b.p. 109.5-110.0° (756 mm), $n^{20}D$ 1.4960, d_4^{20} 0.8670]. For identification, the dinitroderivative with m.p. 69-70° was prepared. A mixed melting point with pure 2,4-dinitrotoluene was not depressed.

7th and 8th fractions. The hydrocarbons of the 7th fraction were combined with the aromatic part (2.29 g) of the 8th fraction, isolated by chromatography on silica gel, and investigated by a spectral method. According to Raman spectrum data, the combined composition was p-xylene 18, m-xylene 40, o-xylene 17 and 1,2,4-trimethylbenzene 25.

The dearomatized part of the 8th fraction (0.61 g) had the following properties: b.p. 191.5-191.8° (754 mm) (by Sivolobov's method), $n^{20}D$ 1.4482, d_4^{20} 0.8139. Comparison of the constants of this fraction with those of 1-methyl-1-butylcyclohexane shows that it was the original hydrocarbon.

The 9th and 10th fractions we considered were mainly the original 1-methyl-1-butylcyclohexane with aromatic hydrocarbons present. By chromatographic adsorption the combined fractions yielded 6.20 g of a naphthene part with constants [b.p. 191.0-191.5° (752 mm), $n^{20}D$ 1.4479, d_4^{20} 0.8142] which corresponded to those of the original hydrocarbon. Besides the naphthene fraction, chromatography yielded 2.55 g of a mixture of aromatic hydrocarbons with b.p. 162.0-175.0°; $n^{20}D$ 1.5035, d_4^{20} 0.8698. The composition of these hydrocarbons was determined by the Raman spectrum. It was found that they were 1,2,4-trimethylbenzene (76%) and 1,3,5-trimethylbenzene (24%).

The residue was not analyzed specially. However, the high boiling point, refractive index and specific gravity indicate that it contained condensed aromatic hydrocarbons.

Table 6 gives the approximate percent composition of the catalysis products of 1-methyl-1-butylcyclohexane, calculated on the hydrocarbon converted (the residue was not considered).

The degree of conversion of the hydrocarbon was 84.2%.

SUMMARY

1. A study was made of the catalytic conversions of 1-methyl-1-propylcyclohexane and 1-methyl-1-butylcyclohexane on an aluminosilicate catalyst at 500°. Under the catalysis conditions chosen, on the aluminosilicate catalyst there occurred elimination of alkyl substituents from the quaternary carbon atom, and the processes of hydrocracking, alkylation, dehydrogenation and isomerization of the six-membered ring into a five-membered one.

2. Aromatic hydrocarbons predominated in the catalysis products but paraffins (mainly gaseous) and five- and six-membered naphthenes were also formed.

When the number of carbon atoms in the alkyl group of gem-methylalkylcyclohexanewas increased, the degree of conversion of the hydrocarbon increased.

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DEMETHYLATION DURING HYDROGENOLYSIS OF FIVE-MEMBERED CYCLANES AND n-ALKANES ON A SKELETAL Ni – Al CATALYST

N. I. Shuikin and M. I. Cherkashin

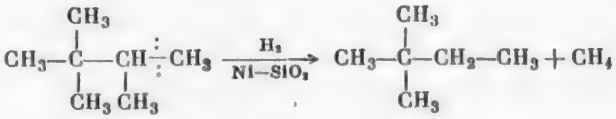
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In 1933 [1] it was found that in contact with platinized charcoal at 300-310° in excess hydrogen, pentamethylene rings were opened with the formation of alkanes. In subsequent investigations [2] it was established that platinized charcoal was a specific catalyst for hydrogenolysis of C-C bonds of a five-membered ring. By studying the effect of the nature of other catalysts on the character of the hydrogenolysis of a pentamethylene ring, it was found [3] that in the presence of a nickel – alumina catalyst isoamylcyclopentane and n-butylcyclopentane underwent extensive conversions even at 250° with the formation of a mixture of low-boiling alkanes and aromatic hydrocarbons.

An attempt to hydrogenolyze cyclopentane in the presence of nickel deposited on kieselguhr [4] established that at 250-300° there was rapid cleavage of the ring with the formation of methane.

Analogous results were obtained [5] when methylcyclohexane was passed over a nickel – alumina catalyst. Hydrogenation of this hydrocarbon at 260° yielded a complex mixture of alkanes, which could not be separated on an efficient column. Such a rapid decomposition of the pentamethylene ring prompted the authors to determine the effect of a nickel – alumina catalyst on the hydrogenolysis of C – C bonds of alkanes. It was found that even at 260° 3-methylpentane was 50% converted into methane.

Somewhat earlier [6] it was shown that in the presence of nickel on deactivated kieselguhr at 240-280°, selective demethylation of branched alkanes occurred with the formation of isoalkanes with shorter chains:



Thus, the investigation of nickel catalysts in the hydrogenolysis of C – C bonds of five-membered cyclanes and alkanes showed that their catalytic properties were determined by the nature of the carrier used. Thus, nickel deposited on aluminum oxide [3, 5] showed no specific action with respect to either five-membered cyclanes or alkanes of various structures, while deposited on deactivated kieselguhr [6] produced selective demethylation of isoalkanes.

In this connection it seemed interesting to study the effect of the skeletal nickel – aluminum catalyst, which is widely used in the laboratory and in industry, on the character of the hydrogenolysis of carbon – carbon bonds of pentamethylene hydrocarbons and alkanes. We were thus able to find comparatively mild conditions for the hydrogenolysis of the pentamethylene ring, accompanied by partial simplification of the molecule of the original hydrocarbon. An investigation of the specific features of the skeletal Ni – Al catalyst showed that it was also capable of producing the successive demethylation of n-alkanes under the same conditions, namely at 200° and normal pressure.

TABLE 1

Properties of Original Hydrocarbons

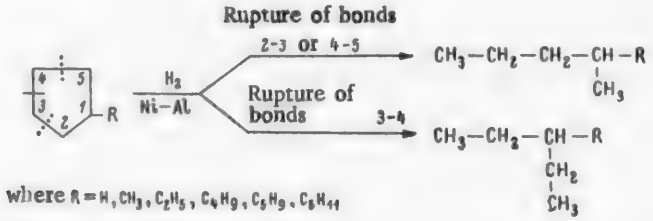
Hydrocarbons	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}
Dicyclopentyl	188—189° (745)	1.4642	0.8650
Isoamylcyclopentane	171.2 (744)	1.4337	0.7875
1-Butylcyclopentene-1	156.5 (748)	1.4488	0.8107
Ethylcyclopentane	102.2 (738)	1.4196	0.7668
Methylcyclopentane	71.2 (748)	1.4101	0.7480
Cyclopentane	48.7 (738)	1.4063	0.7452
n-Hexane	68.0 (760)	1.3750	0.6594
n-Heptane	98.0 (760)	1.3877	0.6836
n-Octane	125.5 (760)	1.3972	0.7024

EXPERIMENTAL

Experiments on the hydrogenolysis of the five-membered ring were carried out with dicyclopentyl, isoamylcyclopentane, 1-butylcyclopentene-1, ethylcyclopentane, methylcyclopentane and cyclopentane at 200° and normal pressure in the presence of a skeletal nickel – aluminum catalyst, from which 10% (catalyst No. 1) and 15% (catalyst No. 2) of the total available aluminum had been removed by treatment with 10% sodium hydroxide solution. The original alloy contained 27% of nickel and 73% of aluminum. The hydrocarbons taken for the investigation were passed through a glass tube with the catalyst in excess hydrogen at a volume rate of 0.06-0.1 hour^{-1}. The properties of the original hydrocarbons are presented in Table 1.

The n-alkanes, n-hexane, n-heptane and n-octane, were hydrogenolyzed in the presence of Ni – Al catalyst No. 2 at 200° and normal pressure and with a volume rate of 0.06 hour^{-1}. The results obtained are presented in Tables 2 and 3, which show that in contrast to nickel on alumina, the skeletal nickel – aluminum catalyst had a definite specific action with respect to the carbon – carbon bonds of both a five-membered ring and of n-alkanes.

Thus, in the hydrogenation of alkylcyclopentanes on a skeletal nickel – aluminum catalyst, even at 200° the five-membered ring was opened at bonds removed from the alkyl substituent with the formation of isoalkanes; no hydrogenolysis of the C – C bonds in the side chain was observed:



Normal hydrocarbons were not found in the catalyzate. Together with the products from opening of the five-membered ring at one C – C bond, hydrocarbons were also formed with one or two CH_2 groups less in their molecule than in the original cyclanes:

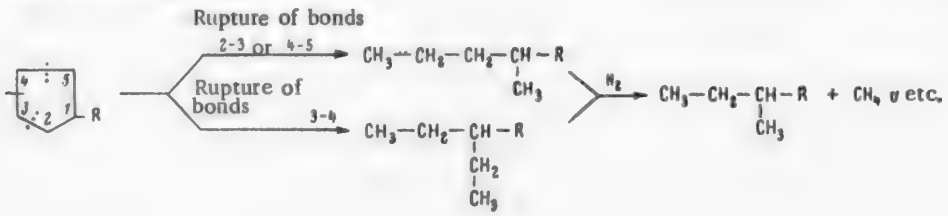


TABLE 2

Hydrogenolysis Products of Hydrocarbons of the Pentamethylene Series at 200° and Normal Pressure

Original hydrocarbon	Ni – Al catalyst number	Degree of hydrogenolysis (in %)	Hydrogenation and hydrogenolysis products isolated and their properties (yields are given in % of catalyzate)
Dicyclopentyl	2	80.3	Low-boiling hydrocarbons (b.p. 50-125.2° at 742 mm, $n^{20}D$ 1.4080, d_4^{20} 0.7326) – 15.5%; isopropylcyclopentane (b.p. 125.2-125.4°, $n^{20}D$ 1.4239, d_4^{20} 0.7717) – 6%; 2-cyclopentylbutane (b.p. 151.2-152°, $n^{20}D$ 1.4348, d_4^{20} 0.7939) – 12.4%; 2-cyclopentylpentane and 3-cyclopentylpentane (b.p. 175-175.6°, $n^{20}D$ 1.4403, d_4^{20} 0.8060) – 13.9%; dicyclopentyl – 27.1%.*
Isoamylcyclopentane	2	73.2	Low-boiling alkanes (b.p. 74-133° at 760 mm), $n^{20}D$ 1.3945, d_4^{20} 0.7000) – 19.1%; 2,5-dimethylheptane (b.p. 133-135°, $n^{20}D$ 1.4046, d_4^{20} 0.7195) – 14.0%; 2,5-dimethyloctane and 2-methyl-5-ethylheptane (b.p. 156.4-157.7°, $n^{20}D$ 1.4133, d_4^{20} 0.7377) – 28.1%; isoamylcyclopentane – 33.5%.
1-Butylcyclopentene-1	2	85	Low-boiling alkanes (b.p. 60-89.5° at 760 mm), – 10.7%; 2-methylhexane (b.p. 89.5-91.5°, $n^{20}D$ 1.3876, d_4^{20} 0.6854) – 4.2%; 3-methylheptane (b.p. 118.3-118.5°; $n^{20}D$ 1.3993, d_4^{20} 0.7080) – 12.1%; 4-methyloctane and 3-ethylheptane (b.p. 140.3-141.5°; $n^{20}D$ 1.4064, d_4^{20} 0.7205) – 16.6%; n-butylcyclopentane – 22.1%.*
Ethylcyclopentane	1	40	3-Methylpentane [b.p. 61.0-63.0° (748.5 mm), $n^{20}D$ 1.3762, d_4^{20} 0.6650] – 3.8%; 3-methylhexane and 3-ethylpentane (b.p. 90.0-93.0°, $n^{20}D$ 1.3912, d_4^{20} 0.6954) – 13.7%; ethylcyclopentane – 67.7%.*
Methylcyclopentane	1	43.0	Isopentane (b.p. 28.0-29.0 at 734 mm, $n^{20}D$ 1.3528, d_4^{20} 0.6193) – 1.7%; 2-methylpentane (b.p. 59.0-60.0°, $n^{20}D$ 1.3718, d_4^{20} 0.6538) – 4.2%; 2-methylpentane and 3-methylpentane (b.p. 60-62.4°, $n^{20}D$ 1.3750, d_4^{20} 0.6580) – 6.8%; methylcyclopentane – 66.8%.
Cyclopentane	1	51.5	n-Pentane (b.p. 35.5-36.0° at 742 mm, $n^{20}D$ 1.3572, d_4^{20} 0.6265) – 34.6%; cyclopentane – 62.6%.

*The hydrocarbons in the intermediate fractions are not given.

TABLE 3

The Products of Demethylation of n-Alkanes on Skeletal Ni – Al Catalyst 2 at Normal Pressure and 200°

Original hydrocarbon	Degree of hydrogenolysis (in %)	Liquid demethylation products (in % of catalyzate)
n-Hexane	58	n-Pentane 24.8, n-hexane 61.9
n-Heptane	57	n-Pentane 8.3, n-hexane 20.7, n-heptane 66.3
n-Octane	50	n-Pentane 3.3, n-hexane 7.1 n-Heptane 14.2, n-octane 67.1

According to this scheme hydrogenolysis of the pentamethylene ring occurs at one C – C bond initially and the isoalkane formed then undergoes successive demethylation of the carbon chain. To prove the mechanism proposed we studied the behavior of n-alkanes under the same conditions as those used for hydrogenolysis of the alkylcyclopentanes (Table 3).

It was established [7] that under the conditions chosen, n-hexane, n-heptane and n-octane underwent successive selective demethylation with the formation of hydrocarbons with a shortened carbon chain.

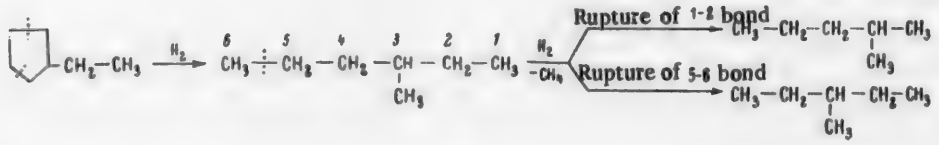
$$CH_3\vdots CH_2-CH_2-CH_2-CH_2-CH_2-CH_2-CH_3 \xrightarrow[-CH_4]{H_2}$$

$$\rightarrow CH_3\vdots CH_2-CH_2-CH_2-CH_2-CH_2-CH_3 \xrightarrow[-CH_4]{H_2}$$

$$\rightarrow CH_3\vdots CH_2-CH_2-CH_2-CH_2-CH_3 \xrightarrow[-CH_4]{H_2} CH_3-CH_2-CH_2-CH_2-CH_3$$

The main hydrogenolysis product of n-hexane was n-pentane. The catalyzate obtained in experiments with n-heptane contained n-hexane in addition to n-pentane. Hydrogenolysis of n-octane led to the formation of n-pentane, n-hexane and n-heptane. The emergent gases contained largely methane.

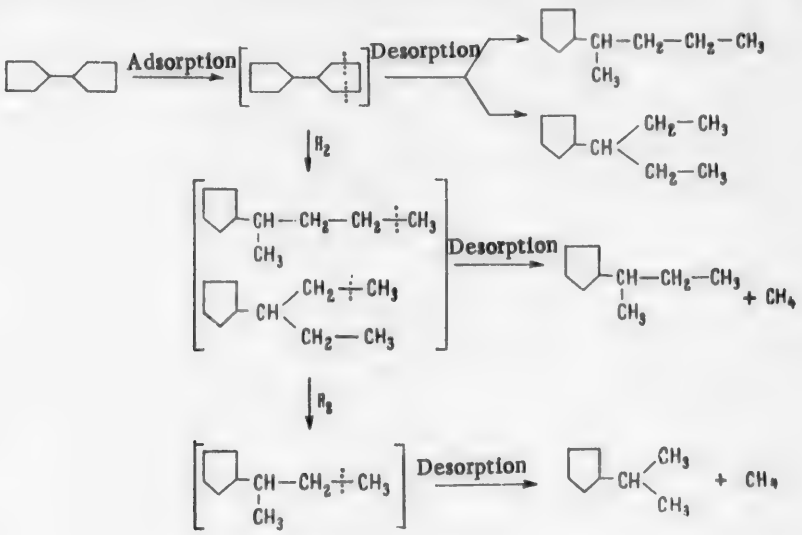
However, the shortening of the carbon chain of alkanes formed by hydrogenolysis of cyclopentane homologs proceeds predominantly at the expense of carbon atoms, which were previously part of the five-membered ring. This is demonstrated by the structure of the isoalkanes formed. Thus, for example, the hydrogenolysis of ethylcyclopentane should yield two hydrocarbons with the carbon chain shortened by one CH_2 group (2-methylpentane and 3-methylpentane), depending on the end of the carbon chain at which demethylation of the initially formed 3-methylhexane occurs:



However, it was found that hydrogenolysis of ethylcyclopentane yielded only 3-methylpentane. Similar results were obtained on investigating the hydrogenolysis of other cyclopentane homologs. Further, experiment showed that under the same conditions the degree of demethylation of alkanes obtained by hydrogenolysis of alkylcyclopentanes was considerably higher than the degree of demethylation of n-alkanes with the same number of carbon atoms. This made it possible to put forward the hypothesis that on the catalyst surface hydrogenolysis first occurs at one C – C bond of the pentamethylene ring and then the isoalkane formed, still remaining in an adsorbed state, undergoes demethylation to lower homologs.

To demonstrate the proposed scheme for the hydrogenolysis of alkylcyclopentanes, we studied the behavior of a hydrocarbon whose alkyl radical had been replaced by a pentamethylene ring.

The results obtained by hydrogenolysis of dicyclopentyl led to the hypothesis that only one pentamethylene ring was adsorbed at first on the catalyst surface, since the hydrogenolysis products contained only alkylcyclopentanes and no alkanes. Here, together with alkylcyclopentanes containing the same number of carbon atoms as dicyclopentyl (2-cyclopentylpentane and 3-cyclopentylpentane), lower homologs, namely 2-cyclopentylbutane and isopropylcyclopentane, were also formed. Since hydrogenolysis of the C – C bonds of the side chain of the alkylcyclopentanes did not occur, evidently the alkylcyclopentanes formed must have undergone demethylation before their desorption from the catalyst surface. Thus, a molecule of dicyclopentyl adsorbed on the surface of the skeletal nickel – aluminum catalyst initially underwent hydrogenolysis at a C – C bond of one of the five-membered rings with the formation of alkylcyclopentanes with the same number of carbon atoms as the original hydrocarbon. These alkylcyclopentanes were partially desorbed from the surface and partially remained on the catalyst surface, undergoing hydrogenolysis to hydrocarbons with a shortened alkyl chain, which then underwent similar conversions as long as there were side chains on the five-membered ring. This route for the formation of alkylcyclopentanes with a shortened chain may be represented by the following scheme:



The results obtained in our work show that the skeletal nickel – aluminum catalyst has a high activity and specificity with respect to the hydrogenolysis of C – C bonds of five-membered cyclanes and alkanes.

SUMMARY

1. It was established that alkylcyclopentanes undergo hydrogenolysis over a skeletal nickel – aluminum catalyst at 200° and normal pressure to form alkanes, which then undergo successive demethylation to lower alkanes under these conditions.

2. It was found that under these conditions the dicyclopentyl molecule undergoes hydrogenolysis at only one pentamethylene ring with the formation of cyclanes with a shorter alkyl chain in addition to isoamylcyclopentanes.

3. Under the same conditions n-alkanes undergo successive demethylation to hydrocarbons with a shorter chain.

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CATALYTIC HYDRODEALKYLATION OF POLYALKYLBENZENES

I. DEMETHYLATION OF TOLUENE ON 10% $Ni - Al_2O_3$. EFFECT OF HYDROGEN PRESSURE

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The national economy's need of benzene, which is one of the most important products in the production of synthetic fibers, plastics, detergents, synthetic dyes etc., is considerably greater at the present time than the need of toluene and certain other benzene homologs. The use of toluene in the civil section of industry is quite limited and the problem of assimilating the excess toluene from both coal-tar and oil sources by its demethylation to give benzene is of undoubted practical interest.

Work begun in 1954 by one of the authors [1-5] on the catalytic conversions of aromatic hydrocarbons (benzene, toluene, ethylbenzene, isopropylbenzene, xylene etc.) under benzine reformation conditions at 460° and 25 and 50 atm. over $Ni - Al_2O_3$ and $Pt - Al_2O_3$ showed that these hydrocarbons underwent extremely varied conversions. Together with their dealkylation, disproportionation of substituents was observed and also hydrogenation to the corresponding six-membered cyclanes with subsequent partial isomerization to five-membered cyclanes and hydrogenolysis of the latter.

Recently work [6-8] has appeared on the catalytic dealkylation and conjugated alkylation of polyalkylbenzene fractions in the presence of benzene or toluene on synthetic $Al_2O_3 \cdot SiO_2$ at 480° and 10-15 atm.

In the last ten years several patents have been taken out on the catalytic dealkylation of benzene homologs over $MgO-Al_2O_3$ [9], $FeF_3-Al_2O_3 \cdot SiO_2$ [10], $Ni-Al_2O_3 \cdot SiO_2$ [11] at temperatures up to 550° and pressures up to 260 atm.

In a voluminous work [12] devoted to the thermal and catalytic dealkylation of both individual aromatic hydrocarbons (toluene, xylenes and methylnaphthalenes) and their concentrates obtained by aromatization of oil fractions it was shown that in the presence of $Cr_2O_3-Al_2O_3$, $MoO_3-Al_2O_3$ and other catalysts at 560-700° and 15-25 atm. together with demethylation there was considerable hydrocracking to methane and noticeable coke formation. In one of the works cited, including the patents, was a study made of the stability of the catalysts since in a series of cases the duration of the experiments did not usually exceed 3 hours [12].

The aim of the present work was to study the conditions of selective conversion of toluene into benzene on an active and quite stable catalyst with little hydrogenation of the benzene nucleus, disproportionation of methyl groups, hydrocracking and thermal decomposition with "coke" formation.

As is known, under a normal pressure of hydrogen and at temperatures of the order of 450° and above there occurs extensive cleavage of toluene and coking up of oxide-metal (platinum, nickel etc.) catalysts. At the same time raising the hydrogen pressure promotes hydrogenation of the benzene ring, which is undesirable in this case. Due to this, in the first instance it seemed necessary to investigate the effect of hydrogen pressure on the demethylation of toluene.

We investigated the demethylation of toluene on samples of finely dispersed nickel, deposited on activated aluminum oxide, at 460°, a volume rate of 0.6 $hour^{-1}$, a molar ratio of hydrogen to toluene of 5:1 and pressures of from 5 to 25 atm.

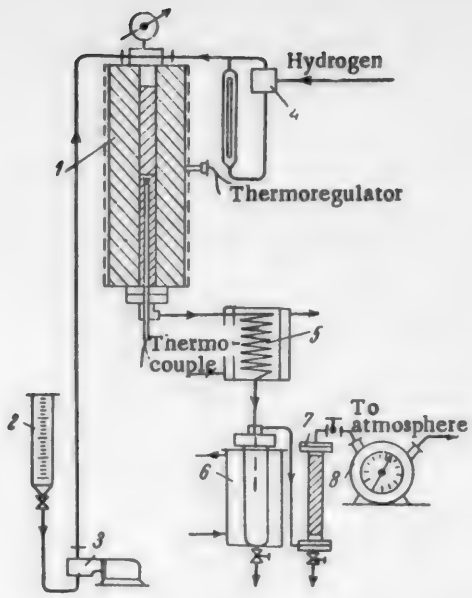


Fig. 1. Plan of apparatus for demethylation of toluene. 1) Reactor, 2) measuring tank, 3) pump, 4) rheometer, 5) cooling condenser, 6) separator – receiver, 7) adsorber, 8) gasmeter.

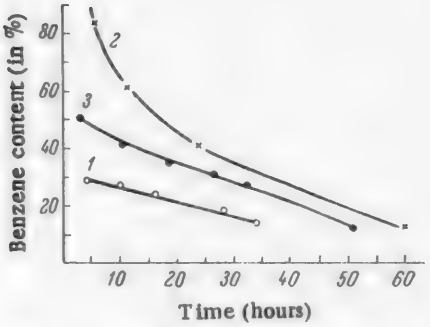


Fig. 2. Change in benzene content of catalyzates in relation to operating time of 10% Ni – Al_2O_3 catalyst. 1) 460°, v 0.5 $hr.^{-1}$, $5H_2$: HC, 25 atm.; 2) 460°, v 0.6 $hr.^{-1}$, $5H_2$: HC, 10 atm.; 3) 460°, v 0.6 hr^{-1}, $5H_2$: HC, 5 atm.

EXPERIMENTAL

Starting Materials. The toluene was chemically pure grade and had b.p. 110-110.5° (746 mm), $n^{20}D$ 1.4970, d_4^{20} 0.8668.

Electrolytic hydrogen, GOST-3022-45, contained 99.7% H_2.

Preparation of Catalyst With the Composition 10% Ni – Al_2O_3. Fired aluminum oxide was impregnated with a molar solution of nickel nitrate, dried and formed into small cylinders 4 × 4 mm in size. The catalyst was then reduced in a stream of hydrogen [13]. The activity of the catalyst was tested by the degree of hydrogenation of benzene at 170-180°. The specific surface of the catalyst was determined by a dynamic method by benzene adsorption and the mechanical strength by the VNII NP (All-Union Sci. Res. Inst. for Petroleum Processing method.*

Analysis of Catalysis Products. The refractive index and the specific gravity of the liquid products were determined and then the catalyzates were fractionally distilled on a column with an efficiency of 42 theoretical plates. The six-membered cyclane content of appropriate fractions was established by their dehydrogenation by Zelinskii's method over 10% Ni – Al_2O_3 at 310° and atmospheric pressure. Separate fractions of the catalyzate were analyzed by their Raman spectra.**

The gaseous catalysis products were analyzed on an Orsat – Lunge apparatus and by chromatography [14].

Apparatus. The experiments were carried out in the flow apparatus illustrated in Fig. 1 and consisted of a block reactor (1) made from an ÉYaIT stainless steel tube 25 mm in diameter and 800 mm high set in an aluminum block fitted with an electrical heater. The temperature of the reactor was regulated automatically with an ÉPV-01 electronic potentiometer. The temperature in the reactor was measured with a chromel-copel thermocouple. The apparatus was fitted with a pump (3) to feed in toluene and a condensing system consisting of a cooling condenser (5) and a separator-receiver (6). The hydrogen was introduced into the reactor from a tank through a rheometer (4).

Experimental Procedure. The reactor was loaded with 100 ml of precatalyst (aluminum oxide cylinders 4 × 4 mm in size), which was to evaporate the toluene and heat the toluene vapors and also the hydrogen. Thus, the vapor – gas mixture entered the catalyst at the required temperature. The catalysis products passed through the condenser (5) into the separator-receiver (6). The catalyzate was trapped in the separator while the gaseous

*Method and apparatus for determining the mechanical strength of catalyst 9882TU of the Ministry of the Petroleum Industry USSR.

**The optical analysis was carried out by Yu. P. Egorov and the authors are very grateful to him.

TABLE 1

Yield and Composition of Catalysis Products (460°; v = 0.6 hour^{-1} and 5H_2 : HC)

Expt. No.	Pressure (in atm.)	Degree of conversion of toluene (in %)	Catalyzate yield (in %)	Comp. catalyzate (in weight %)		Benzene yield (in mole %)		Ch_4 yield on toluene demeth. (in mole %)
				benzene	cyclanes	on toluene passed	on toluene converted	
1	25	46.0	88.5	29.4	10.7	30.5	66.5	183.0
3	25	39.4	89.6	21.4	9.0	22.6	57.2	128.0
4	25	38.8	88.7	23.0	7.6	24.0	62.2	193.0
5	25	36.0	86.6	18.1	7.5	18.5	51.2	178.0
8	10	63.0	76.4	51.5	—	46.0	73.0	221.0
10	10	60.0	72.0	43.6	—	37.0	61.5	265.0
12	10	52.0	77.5	38.0	—	34.6	66.0	275.0
14	5	59.3	81.0	49.5	—	47.2	80.0	81.2
16	5	45.6	87.0	37.8	—	38.8	85.0	93.0
17	5	43.0	84.3	32.7	—	32.4	75.5	73.5

TABLE 2

Fractional Composition of Catalyzates and Composition of Gaseous Catalysis Products

Expt. No.	Pressure (in atm.)	Catalyzate properties		Boiling point of fractions at 744 mm	Content (in wt.%)	Comp. gases (in volume %)	
		n_D^{20}	d_4^{20}			hydrogen	methane
4	25	1.4915	0.8602	79—79.5°	29.0	90.0	10.0
				79.5—109	3.6		
				109—109.5	62.2		
				Residue	2.8		
				Losses	2.4		
12	10	1.4985	0.8733	79.5—80	43.5	80.0	20.0
				109—110	53.5		
				Residue	1.5		
				Losses	1.5		
17	5	1.4976	0.8730	79—80	32.7	95.0	5.0
				109—110	63.6		
				Residue	2.2		
				Losses	1.5		

products passed through the adsorber (7) filled with activated charcoal into a gasmeter (8) and then into the atmosphere.

The toluene was first passed over the catalyst for 1-2 hours (preexperiment period); during this time the toluene input rate, temperature and pressure were established. When the catalyzate that accumulated in the receiver during the preexperiment period had been removed, experiments were carried out for long-term testing of the activity and stability of the catalysts. Three series of experiments were carried out on the catalytic demethylation of toluene at 460°, a volume rate of 0.6 hour^{-1}, a molar ratio of hydrogen to toluene of 5H_2 : HC and various hydrogen pressures, namely 25, 10 and 5 atm. A freshly prepared sample of 10% Ni – Al_2O_3 was used for each series of experiments, which included from 4 to 8 experiments of 5 hours duration. For each series of experiments, a material balance was drawn up of the starting materials and the final catalysis products. The losses during the experiments usually did not exceed 2-3%.

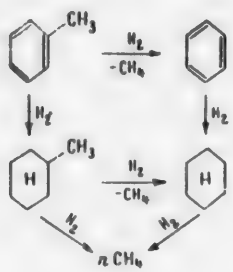
The results of the experiments are given in Table 1 and illustrated in Fig. 2. The characteristics of the catalyzates and also the results of their fractional distillation and the composition of the gaseous catalysis products for the most characteristic experiments of all three series are given in Table 2.

As follows from the data in Table 1, the degree of conversion of toluene in experiments at 25 atm. (experiments 1, 3, 4 and 5) was on an average 40%, at 10 atm. (experiments 8, 10 and 12), 59% and at 5 atm. (experiments 14, 16 and 17), 49%. The catalyzate yields in experiments at 25 atm. were highest (experiment 3) (89.6%), while in experiments at 10 atm. the yields were not greater than 77% (experiment 12). The yield of benzene on the toluene converted was highest in the last series of experiments and reached 85% (experiment 16).

In individual cases, the hydroaromatic hydrocarbon content of the catalyzates obtained in experiments at 25 atm. exceeded 10% (experiment 1). As analysis data showed, these hydrocarbons consisted of 90% cyclohexane and 10% methylcyclohexane. The catalyzates obtained in experiments at 5 and 10 atm. contained only traces of hydroaromatic hydrocarbons. The disproportionation of methyl groups did not occur among the conversions of toluene as the presence of xylenes was not detected in the catalyzates.

Analysis of the gaseous catalysis products showed that besides hydrogen there was only methane, whose content varied considerably, depending on the experimental conditions. While in experiments at 10 atm. the methane content of the gases reached 20% (experiment 12, Table 2), in experiments at other pressures the gaseous products contained not more than 5-10% methane. This considerable methane content of the gases produced in experiments at 10 atm. pressure indicated considerable hydrocracking of toluene and its conversion products to methane. Thus, in experiment 12 (Table 1) the yield of methane reached 275 mole % on the toluene demethylated. At the same time, in experiments 14, 16 and 17 at 5 atm., hydrogenolysis of hydrocarbons to methane was not observed.

The general scheme for toluene conversions may be represented in the following form:



The "life" of the catalyst for experiments at 25 atm. was 35 hours, at 10 atm., 60 hours and at 5 atm., 50 hours (Fig. 2). The activity of the catalyst fell gradually as is shown by the slopes of the curves in Fig. 2. The lower limit for the benzene content of the catalyzate was arbitrarily taken as 10-12%: when such a benzene content was reached, the catalyst was considered deactivated. At the end of each series of experiments the coke content of the spent catalyst was determined and, for example, in experiment series 2 and 3 this equalled 5.12 and 4.66%, respectively. In these experiments, the amount of toluene broken down to carbon was not more than 0.2% of the total amount of toluene passed over the catalyst.

As the results of determining the specific surface of fresh catalyst and catalyst spent in the third series of experiments showed, the specific surfaces were 211.5 and 161.4 m^2/g, respectively, i.e., a fall of approximately 24%. Samples of the same catalyst (i.e., fresh and spent) were tested for mechanical strength, which was found to be 8100 g for fresh and 6192 g for spent catalyst.

Comparison of the results of all three series of experiments shows that the optimal conditions for selective hydrogenolysis of the methyl group of toluene with the formation of benzene on 10% Ni – Al_2O_3 lay in the low-pressure region (up to 5 atm.). A further decrease in the pressure in the system led to a fall in the hydrogen concentration and consequently the hydrogen did not restore the activity of the catalyst. At 5 atm., 460°, $\underline{v}$ 0.6 $hour^{-1}$ and $5H_2$: HC, with the practically complete absence of hydrogenation of the benzene ring, disproportionation of substituents and hydrocracking, high yields (up to 85%) of benzene on the toluene converted were attained and also a degree of conversion which reached 50%. The catalyzate contained practically only benzene and toluene. The absence of other hydrocarbons from the catalyzate could considerably facilitate the separation of benzene and toluene by continuous distillation.

Under these conditions, the operating period of the catalyst without regeneration reached 50 hours, while its activity fell smoothly.

SUMMARY

1. It was shown that in a flow apparatus at 5 atm. pressure, 460°, a volume rate of 0.6 hour^{-1} and $5H_2$: HC over a 10% Ni – Al_2O_3 catalyst, the demethylation of toluene to benzene proceeded without the formation of hydroaromatic hydrocarbons, disproportionation of methyl groups or hydrocracking of the benzene nucleus to methane. The yield of catalyzate, containing up to an average of 30% of benzene, was about 85% on the toluene passed.

2. At 25 atm., 460°, v 0.6 hour^{-1} and $5H_2$: HC, in addition to demethylation of toluene there was considerable formation of hydroaromatic hydrocarbons (cyclohexane and methylcyclohexane) and also hydrocracking of toluene. At 10 atm. pressure with the other reaction conditions the same, the formation of hydroaromatic hydrocarbons was suppressed, but the hydrocracking of toluene to methane and demethylation of toluene proceeded more rapidly.

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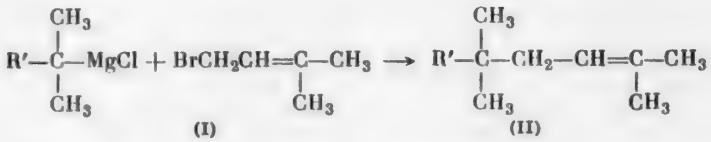
SYNTHESIS OF HYDROCARBONS

LXIX. NEW GENERAL METHOD OF SYNTHESIZING DINEOALKYLS ($C_{10}H_{22} - C_{12}H_{26}$) – DINEOPENTYL AND ITS HOMOLOGS

R. Ya. Levina, P. A. Kaikaris, I. Baukh and E. G. Treshchova

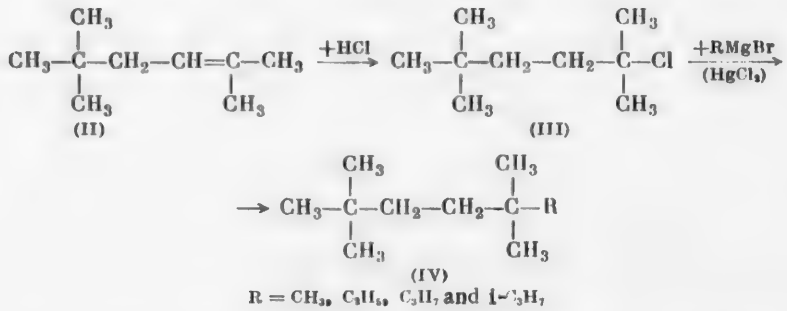
Moscow State University

In our previous communications [1, 2] we described the synthesis of ethylene hydrocarbons with a quaternary carbon atom (II) by the Grignard – Wurtz reaction by the interaction of tertiary-alkylmagnesium chlorides with the primary hydrobromide of isoprene (I).



In the present work, one of these ethylene hydrocarbons, 2,2,5-trimethylhexene-4 [(II), R' = CH_3], obtained by the action of primary hydrobromide of isoprene on tert -butylmagnesium chloride (14% yields),* was used for the synthesis of difficultly accessible paraffinic hydrocarbons with two quaternary carbon atoms separated by two CH_2 groups, i.e., dineopentyl and its homologs (dineoalkyls).

2,2,5-Trimethylhexene-4 (whose structure was confirmed by ozonization and plotting the Raman spectrum) was treated with hydrogen chloride and converted into the tertiary chloride (III) (already containing one quaternary carbon atom, 95% yield), which was then reacted with alkylmagnesium bromides in the presence of mercuric chloride; this second Grignard – Wurtz reaction led to the formation of dineoalkyls (IV).



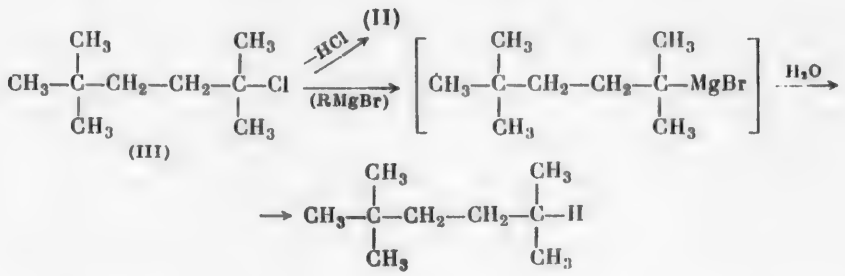
*In the Grignard – Wurtz reaction between isoprene hydrobromide and tertiary-butylmagnesium chloride there are side reactions: on the one hand, the primary hydrobromide of isoprene loses hydrogen bromide to form isoprene and its dimer and on the other, it exchanges its bromine atom for an MgCl group to form a new organomagnesium compound of the allyl type; interaction of the latter with isoprene hydrobromide, reacting in its two isomeric forms, leads to the formation (in a total yield of 16.5%) of isomeric $C_{10}H_{18}$ diene hydrocarbons with isolated double bonds, namely 2,7-dimethyloctadiene-2,6 (6.5%) and 2,5,5-trimethylheptadiene-2,6 (10%).

Raman Spectra of $C_{10} - C_{12}$ Dineoalkyls*

2,2,5,5-Tetramethylhexane	2,2,5,5-Tetramethylheptane	2,2,5,5-Tetramethyloctane	2,2,5,5,6-Pentamethylheptane
229 (5), 295 (4)	224 (2.5, w), 269 (0.5)	234 (4, w), 295 (3, w)	232 (3.5, w), 293 (2, w)
329 (1.5)	307 (1.5), 333 (1.5, d)	333 (3)	340 (2)
356 (0)	370 (0.5)	358 (0.5)	387 (1.5)
406 (2.5)	406 (2.5), 416 (0)	413 (2)	420 (1)
444 (0.5)	455 (0.5)	439 (0.5), 460 (0.5)	457 (0.5), 473 (0.5)
502 (4.5)	504 (6)	497 (3, w)	498 (3.5)
586 (0.5)	547 (1)	547 (1.5), 603 (0)	546 (1.5), 586 (0)
650 (1), 699 (0.5, w)	697 (0.5)	691 (0)	693 (3.5), 700 (0.5)
764 (6, w)	718 (4), 746 (10, w	746 (2.5/b), 764 (2/b	753 (4, w), 769 (1 w)
—	816 (0), 833 (0)	788 (2.5), 820 (0)	832 (0.5)
861 (0.8), 875 (0.5)	862 (2), 884 (2)	862 (0.5), 882 (2.5)	859 (1), 875 (1)
912 (8), 930 (5)	912 (10), 930 (10)	912 (3), 930 (3.5)	912 (8), 932 (4)
—	956 (1), 996 (0.5)	965 (0.5), 995 (0.5)	958 (2, d), 995 (1)
1016 (1.5)	1012 (6), 1046 (1)	1015 (0.5), 1040 (3)	1015 (0.5), 1046 (1)
1064 (1.5), 1093 (1)	1065 (4)	1081 (1), 1090 (1.5, w)	1080 (2), 1100 (1.5)
1144 (4), 1170 (0.5)	1133 (5)	1140 (3, w) 1170 (0.5)	—
1194 (4), 1219 (4, w)	1196—1204 (10, w, b)	1198 (7, w/b), 1222 (0.5)	1196 (3, w, 1219 (3.5, w)
1253 (8)	1246 (8)	1250 (4)	1250 (7), 1267 (0.5)
—	1309 (0.5)	1295 (0.5)	1296 (0.5)
1327 (4)	1323 (1.5)	1323 (3, w)	1323 (2.5, d)
1354 (1), 1382 (1)	1347 (1.5), 1354 (1), 1384 (2)	1354 (1.5), 1383 (1.5)	1358 (1), 1390 (0.5)
1443 (10/b), 1462 (6/b)	1443 (20), 1467 (12)	1440 (10), 1461 (2.5)	1443 (10), 1464 (4)

* w = wide, b = background, d = double.

When the tertiary chloride (III) was reacted with alkylmagnesium bromides, there were also side reactions: hydrogen chloride was eliminated from the tertiary chloride (with the formation of ~50% of the original 2,2,5-trimethylhexene-4), which was also reduced to 2,2,5-trimethylhexane.



The mixture of dineoalkyl and the lower-boiling trimethylhexene and trimethylhexane formed in each case was separated by distillation on a column (after hydrochlorination, the trimethylhexene was again used for the synthesis of dineoalkyls). The dineoalkyls obtained were distilled on a column of 35 theoretical plates and purified by chromatography on silica gel; their yields were 10-16% calculated on the tertiary chloride (III) taken or 20-32% on that which underwent the Grignard – Wurtz reaction. A study of the Raman spectra of the hydrocarbons obtained confirmed that they contained quaternary carbon atoms since the spectra contained intense lines in the region of 912-932 and 1200-1250 cm^{-1}.

Thus, dineopentyl and its homologs may be synthesized from isoprene by the following general method: hydrobromination of isoprene, replacement of the labile bromine atom of the hydrobromide (by the Grignard – Wurtz reaction) by a tertiary-butyl group, hydrochlorination of the alkene with one quaternary carbon atom thus formed and subsequent replacement of the chlorine atom in the tertiary chloride formed (by a second Grignard – Wurtz reaction) by an alkyl group.

Of the dineoalkyls synthesized in the present work by the "two-fold Grignard – Wurtz reaction", the literature describes only the first member of the series, namely dineopentyl (2,2,5,5-tetramethylhexane); it was

synthesized by other and more or less complicated methods, namely, by the action of sodium on neopentyl chloride [3, 4], by the electrolysis of sodium tertiary-butylacetate [4], by exhaustive hydrogenation of 2,2,5,5-tetramethylhexyne-3 (obtained by a five-stage synthesis from pinacone [5]) etc. [6, 7].

EXPERIMENTAL

2,2,5-Trimethylhexene-4 was synthesized in 14% yield by the reaction of the primary hydrobromide of isoprene with tertiary-butylmagnesium chloride by the method described previously [1] with the only difference that the isoprene hydrobromide was added to the tertiary-butylmagnesium chloride with snow and salt cooling (from -5 to -8° in the reaction mixture).

After the usual processing, boiling with sodium, distillation over the latter, and two distillations on a column* (of 35 theoretical plates), the hydrocarbon had the following constants:

B.p. 126.5-127° (740 mm), $n^{20}D$ 1.4219, d_4^{20} 0.7370, MR_D 43.49. $C_9H_{18}F$. Calculated 43.29.

Literature data [8]: b.p. 126.7° (760 mm), $n^{20}D$ 1.4210, d_4^{20} 0.7335.

The Raman spectrum of 2,2,5-trimethylhexene-4 contained the frequency 1669 cm^{-1}, which is characteristic of a double bond in a trisubstituted ethylene (the intensities of the spectral lines are given with respect to an arbitrary scale in which the intensity of the line at 1442 cm^{-1} is taken as 10 units):

246 (2.5, broad), 295 (0.5), 310 (4.5, broad), 354 (0.5), 387 (2), 420 (1), 440 (2.5), 494 (4), 528 (2), 580 (0), 603 (0), 635 (4), 693 (3), 718 (0), 740 (20), 753 (1.5), 788 (0), 845 (1), 862 (1.5), 904 (1), 909 (4.5), 930 (8), 956 (0), 1008 (0.5), 1033 (0.5), 1046 (1), 1076 (1), 1102 (2, diffuse), 1117 (2), 1144 (8, broad), 1170 (0.5 background), 1189-1196 (4, double/background), 1219 (0.5), 1240 (5), 1272 (2), 1300 (5), 1352 (1), 1380 (6), 1415 (0.5), 1442 (10), 1460 (2.5 background), 1669 (25).

2,2,5-Trimethylhexene-4 (5 g) was ozonized under the usual conditions. After evaporation of the solvent (chloroform) in vacuum (without heating), the ozonide was boiled for a few hours with water and 10% hydrogen peroxide. The reaction mixture was neutralized with sodium carbonate and the acetone peroxide (m.p. 131°; literature data [10]: m.p. 131-133°) and acetone (identified by preparation of the 2,4-dinitrophenylhydrazone with m.p. 125°; mixed melting point not depressed) steam distilled from it. The solution of acid salts remaining in the distillation flask yielded tertiary-butylacetic acid, which was identified as the amide with m.p. 130-131° (literature data [11]: m.p. 132°).

Hydrochlorination of 2,2,5- trimethylhexene -4 was carried out by saturating the substance with hydrogen chloride with cooling (ice and salt) and then shaking the material for 2-3 days at room temperature with a three-fold volume of concentrated hydrochloric acid, first saturated with hydrogen chloride at -10°. The tertiary chloride formed, 5-chloro-2,2,5-trimethylhexane (not described in the literature), was separated from the hydrochloric acid solution, washed with water, dried with calcium chloride and distilled (yield 85%).

B.p. 88-90° (60 mm), $n^{20}D$ 1.4335, d_4^{20} 0.8687, MR_D 48.71. $C_9H_{19}Cl$. Calculated 48.63.

Found %: C 66.63, 66.82; H 11.98, 12.05; Cl 21.49, 21.01. $C_9H_{19}Cl$. Calculated %: C 66.44; H 11.74; Cl 21.82.

On distillation and storage, the chloride readily lost hydrogen chloride.

We also collected a low-boiling fraction (13%) with b.p. 125-127° (750 mm) and $n^{20}D$ 1.4220, which was the original 2,2,5-trimethylhexene-4.

Synthesis of 2,2,5,5-Tetramethylalkanes (dineoalkyls). To an ether solution of alkylmagnesium bromide (1.65 mole of alkyl bromide, 36 g of magnesium and 450 ml of absolute ether) was added 4 g of mercuric chloride; the reaction mixture was heated until the mercuric chloride dissolved completely and then cooled to

*In the first distillation of the reaction products on a column, the low- and high-boiling fractions were also collected; the latter were the side products 2,5,5-trimethylheptadiene-2,6 (10% yield) with b.p. 148.5-149.5° (751 mm), $n^{20}D$ 1.4400, d_4^{20} 0.7653 and 2,7-dimethyloctadiene-2, 6 (6.5% yield) with b.p. 165.7-166.5°) 748 mm), $n^{20}D$ 1.4472, d_4^{20} 0.7750. Literature data [9]: b.p. 149.7° (760 mm), $n^{20}D$ 1.4371, d_4^{20} 0.7657 and b.p. 168.6° (760 mm), $n^{20}D$ 1.4478, d_4^{20} 0.7755. The low-boiling fraction yielded hexamethylethane (di-tertiary-butyl) with b.p. 106-107° (726 mm) and m.p. 102°.

12-14° and to it was slowly (over a period of 6 hours) added an ether solution (1 : 1) of the tertiary chloride 5-chloro-2,2,5-trimethylhexane (0.75 mole). Stirring was then continued for 3 hours at room temperature and 3 hours with heating; the reaction mixture was decomposed by gradually pouring it onto ice and then adding 2 N hydrochloric acid. After removal of the ether from the washed and dried ether extracts, the residue was shaken 2-3 times with hot, concentrated hydrochloric acid (to decompose the organomercury compound formed), then washed with water, sodium carbonate solution and again with water and dried with calcium chloride. In the first distillation (with a still head) we collected the low-boiling fraction of the original 2,2,5-trimethylhexene-4 with some 2,2,5-trimethylhexane (125-128°; yield ~50% in reactions with various alkylmagnesium bromides; this was again used for preparing the tertiary chloride 5-chloro-2,2,5-trimethylhexane) and the dineoalkyl fraction, which was then boiled over sodium until the halide disappeared completely and fractionated on a column of 35 theoretical plates. The dineoalkyl isolated was redistilled on a column and purified by chromatography on silica gel.

2,2,5,5-Tetramethylhexane [dineopentyl (IV), R = CH_3; yield 16 g 15%]. The purity of the preparation* was 97 mol % (solid. pt. -17°) and after freezing, 98.5 mole % [it is possible that it contained 2,2,5-trimethylhexane with b.p. 123.5° (750 mm) [1], which was not removed by chromatography]:

B.p. 135-135.5° (735 mm), $n^{20}D$ 1.4064, d_4^{20} 0.7212, MR_D 48.52. $C_{10}H_{22}$. Calculated: 48.38.

Literature data [6]: b.p. 137.4° (760 mm), $n^{20}D$ 1.4055, d_4^{20} 0.7187.

2,2,5,5-Tetramethylheptane [(IV), R = C_2H_5]; not described in the literature; yield 18.7 g (16%), purity of preparation 99.4 mole % (solid. pt. -87.4°).

B.p. 161.8-162° (756 mm), $n^{20}D$ 1.4174, d_4^{20} 0.7426, MR_D 52.98; calc. 52.99.

Found %: C 84.61, 84.69; H 15.57, 15.42. $C_{11}H_{24}$. Calculated %: C 84.52; H 15.48.

2,2,5,5-Tetramethyloctane [(IV), R = C_3H_7]; not described in the literature; yield 19.1 g (15%).

B.p. 180° (739 mm), $n^{20}D$ 1.4213, d_4^{20} 0.7493, MR_D 57.66; calc. 57.62.

Found %: C 84.60, 84.66; H 15.35, 15.26. $C_{12}H_{26}$. Calculated %: C 84.61; H 15.39.

2,2,5,5,6-Pentamethylheptane [(IV), R = iso-C_3H_7]; not described in the literature; yield 12.7 g (10%).

B.p. 179.5-180° (749 mm), $n^{20}D$ 1.4255, d_4^{20} 0.7583, MR_D 57.46; calc. 57.62.

Found %: C 84.70, 84.80; H 15.38, 15.24. $C_{12}H_{26}$. Calculated %: C 84.61; H 15.39.

The Raman spectra of the dineoalkyls synthesized ($C_{10} - C_{12}$) were plotted on a glass three-prism spectrograph (ISP-51) with a slit width of 6 cm^{-1}. The frequencies were determined by linear interpolation from the lines of a standard iron spectrum; the accuracy of the determination ± 1-2 cm^{-1}. The intensities of the lines were evaluated visually according to an arbitrary scale (on which 10 or 20 units were taken as the intensity of the line in the region of ~1450 cm^{-1}). All the dineoalkyls examined (see table) were characterized by intense lines in the region of 718-764 cm^{-1}, i.e., fully symmetrical vibration frequencies of a carbon chain; the presence of intense lines in the regions of 912-932 and 1200-1250 cm^{-1} indicated the complex branching of the chain (with a quaternary carbon atom).

The spectrum of dineopentyl was measured photometrically; the intensities were obtained according to an objective CGS scale, where the integral intensity of the 802-CGS line was taken as equal to 500 units/mole and cm^{-1}.

229 (98), 295 (98), 329 (40), 356 (0), 406 (64), 444 (15), 502 (125), 586 (10), 650 (30), 699 (15, broad), 764 (310, broad), 861 (25), 875 (15), 912-930 (440, double), 1016 (48), 1064 (85), 1093 (60), 1144 (395), 1170 (30), 1194-1219 (560, double), 1253 (386), 1327 (276), 1354-1382 (238, diffuse), 1443-1462 (615, double).

SUMMARY

1. A new general method was developed for synthesizing paraffinic hydrocarbons with two quaternary carbon atoms separated by two CH_2 groups (dineoalkyls). The method consisted of the following successive

*The purity of the crystallizable hydrocarbons was determined by the procedure described in paper [12].

reactions: hydrobromination of isoprene, a Grignard – Wurtz reaction between the primary hydrobromide of isoprene and tertiary butylmagnesium chloride, hydrochlorination of the 2,2,5-trimethylhexene-4 formed and a second Grignard – Wurtz reaction (in the presence of mercuric chloride) between the saturated tertiary chloride obtained (5-chloro-2,2,5-trimethylhexane) and alkylmagnesium bromides.

2. By this method of a "two-fold Grignard – Wurtz reactions," we synthesized the difficultly accessible 2,2,5,5-tetramethylhexane (dineopentyl) and its $C_{11}H_{24}$ and $C_{12}H_{26}$ homologs that have not been described in the literature, namely 2,2,5,5-tetramethylheptane, 2,2,5,5-tetramethyloctane and 2,2,5,5,6-pentamethylheptane.

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CONDENSATION OF HALONAPHTHALIC ANHYDRIDES WITH RESORCINOL

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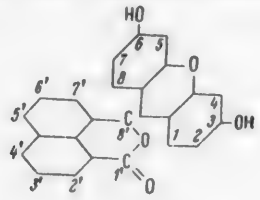
Poltava State Pedagogical Institute

Naphthalfluorescein (I) was obtained by Terrisse [1] by condensing naphthalic anhydride with resorcinol in the presence of anhydrous zinc chloride. He also prepared naphthal-2,4,5,7-tetrabromofluorescein (VIII), but did not give the melting point. Dziewonskii and Zakrzewska-Baranowska [2] studied the condensation of 4-chloronaphthalic anhydride with resorcinol. However they did not give the yield or the melting point of the 5'-chloronaphthalfluorescein (II) thus obtained. There are no literature data on the condensation of 4-bromonaphthalic anhydride with resorcinol or on bromo and iodo derivatives of 5'-chloro- and 5'-bromonaphthalfluoresceins.

We established that the best yield of the halonaphthalfluoresceins listed above was obtained if the condensation reaction was carried out at 180-185° in the presence of anhydrous zinc chloride for 30-40 minutes. Under these conditions, 35-40% of the halonaphthalic anhydrides reacted and the yield of halonaphthalfluoresceins was 70-74% on the anhydride reacted. On raising the temperature to 200-210°, the amount of anhydride reacting increased but the yield of fluoresceins decreased since many tarry materials were formed. Tar formation was also promoted by a large excess of zinc chloride.

The tetrabromo and tetraiodo derivatives (of the eosin and erythrosin type) were readily obtained by bromination and iodination of the halonaphthalfluoresceins obtained. The absorption maxima of the sodium salts of these dyes were shifted into the long-wave part of the spectrum in comparison with eosin and erythrosin:•

	λ mμ (water)
Eosin	516 [3]
Naphthal-2,4,5,7-tetrabromofluorescein	540
5'-Chloronaphthal-2,4,5,7-tetrabromofluorescein	543
5'-Bromonaphthal-2,4,5,7-tetrabromofluorescein	544
Erythrosin	524 [4]
5'-Bromonaphthal-2,4,5,7-tetraiodofluorescein	547
Naphthal-2,4,5,7-tetraiodofluorescein	548
5'-Chloronaphthal-2,4,5,7-tetraiodofluorescein	553



(I) 5' = H, 2, 4, 5, 7 = H
(II) 5' = Cl, 2, 4, 5, 7 = H
(III) 5' = Br, 2, 4, 5, 7 = H
(IV) 5' = Cl, 2, 4, 5, 7 = Br
(V) 5' = Cl, 2, 4, 5, 7 = I
(VI) 5' = Br, 2, 4, 5, 7 = Br
(VII) 5' = Br, 2, 4, 5, 7 = I
(VIII) 5' = H, 2, 4, 5, 7 = Br
(IX) 5' = H, 2, 4, 5, 7 = I

The corrected melting points of the products obtained are presented in the experimental section.

•The absorption maxima of the dyes we obtained were determined in the Kharkhov University laboratory by B. M. Krasovitskii, to whom the authors are grateful.

EXPERIMENTAL

5'-Chloronaphthalfluorescein (II). A mixture of 4.65 g of 4-chloronaphthalic anhydride and 4.4 g of resorcinol was heated to 180° in a porcelain beaker, 4.8 g of anhydrous zinc chloride added and heating continued for 30 minutes at 180-185°. The melt obtained was boiled with 50 ml of water, acidified with hydrochloric acid, collected by filtration, washed with water and dried. The dried product was boiled for 30 minutes with 100 ml of methyl alcohol. The cooled mixture was filtered. 2.8 g of unreacted anhydride remained on the filter. Alcohol (75 ml) was distilled from the filtrate and the residue left for the product to crystallize. The precipitated crystals were collected, washed with 5-6 ml of alcohol and dried. The yield of (II) was 2.3 g (69.5% on the anhydride reacted). The substance crystallized from methyl alcohol in the form of yellow needles with m.p. 293-294°. It was readily soluble in acetone, alcohol and tetrachloroethane. An alkaline solution gave a strong green fluorescence.

Found %: Cl 8.37, 8.41. $C_{24}H_{13}O_5Cl$. Calculated %: Cl 8.52.

5'-Bromonaphthalfluorescein (III) was prepared similarly to (II). From 5.54 g of 4-bromophthalic anhydride we obtained 2.33 g of (III) (74% calculated on the anhydride reacted). The product crystallized from methyl alcohol in the form of yellow needles with m.p. 312-313°. It was soluble in the same solvents as (II).

Found %: Br 17.21, 17.27. $C_{24}H_{13}O_5Br$. Calculated %: Br 17.32.

5'-Chloronaphthal-2,4,5,7-tetrabromofluorescein (IV). 4.17 g of (II) was suspended in 45 ml of methyl alcohol, 3.2 ml of bromine added with stirring and the mixture left at room temperature for 2 hours. The precipitated crystals were collected, washed with 5-6 ml of methyl alcohol and dried. We obtained 7.05 g of (IV) (96%). The product crystallized from bromobenzene in the form of pale pink plates with m.p. 331-332°. It was readily soluble in tetrachloroethane and bromobenzene.

Found %: Cl 4.75, 4.70; Br 43.00, 43.31. $C_{24}H_9O_5ClBr_4$. Calculated %: Cl 4.84; Br 43.69.

Sodium Salt of (IV). (IV) was ground with the calculated amount of anhydrous sodium carbonate, a small amount of 80% alcohol added and the mixture heated on a water bath until the evolution of carbon dioxide ceased. Alcohol was added to the solution obtained until crystallization began and then the solution was left for a day for the product to crystallize. The precipitated crystals of the sodium salt appeared as red needles, which were readily soluble in water, but difficultly so in alcohol. The yield was almost quantitative. The substance dyed silk to a pink color and stained histological preparations (cell nuclei, nerve fibers).

5'-Chloronaphthal-2,4,5,7-tetraiodofluorescein (V). 4.17 g of (II) was dissolved in 45 ml of 2 N potassium hydroxide solution and 150 ml of water added. The solution obtained was heated to 70° and a solution of iodine in potassium iodide added in small portions until the fluorescence disappeared. After 12-20 minutes, the solution was acidified with 2 N hydrochloric acid until a precipitate appeared and left for 2-3 hours. The precipitate was collected, washed with an aqueous solution of potassium iodide and dried. The dry product was treated with 20 ml of ethyl acetate. We isolated 8.1 g (V) (88%) as a yellow powder. It crystallized from bromobenzene as platelets with a pink tinge. The m.p. was 277-278°.

Found %: Cl 3.75, 3.90; I 55.30, 55.47. $C_{24}H_9O_5ClI_4$. Calculated %: Cl 3.86; I 55.17.

The sodium salt of (V) was obtained analogously to the sodium salt of (IV). It crystallized from aqueous alcohol in the form of red needles. The product dyed silk to a pink color.

5'-Bromonaphthal-2,4,5,7-tetrabromofluorescein (VI) was obtained analogously to (IV); the yield was 84%. The product crystallized from bromobenzene as pale pink platelets. The m.p. was 358-360°.

Found %: Br 51.12, 51.80. $C_{24}H_9O_5Br_5$. Calculated %: Br 51.42.

Sodium Salt of (VI). The product formed red needles from aqueous alcohol. It dyed silk and histological preparations.

5'-Bromonaphthal-2,4,5,7-tetraiodofluorescein (VII) was obtained analogously to (V); the yield was 90%. The substance crystallized from bromobenzene as pink platelets. The m.p. was 281-282°.

Found %: Br 8.35, 8.50; I 52.50, 52.95. $C_{24}H_9O_5BrI_4$. Calculated %: Br 8.29; I 52.63.

The sodium salt of (VII) crystallized in the form of red needles. It dyed silk to a pink color.

Naphthal-2,4,5,7-tetrabromofluorescein (VIII) was obtained similarly to (IV); the yield was 96%. The substance crystallized from chlorobenzene as pink platelets. The m.p. was 323-324°.

Found %: Br 45.55, 45.90. $C_{24}H_{10}O_5Br_4$. Calculated %: Br 45.85.

The sodium salt of (VIII) was obtained similarly to the previous ones. It dyed silk and histological preparations. The yield was almost quantitative.

Naphthal-2,4,5,7-tetraiodofluorescein (IX) was obtained similarly to (V); the yield was 90%. The pink platelets had m.p. 293-294° (from chlorobenzene).

Found %: I 56.96, 57.21. $C_{24}H_{10}O_5I_4$. Calculated %: I 57.34.

The sodium salt of (IX) was obtained similarly to the previous ones. The yield was almost quantitative. The product dyed silk to a pink color.

SUMMARY

A study was made of the conditions for condensing monohalonaphthalic anhydrides with resorcinol. We obtained the previously undescribed 5'-bromonaphthalfluorescein and 5'-chloro-2,4,5,7-tetrabromo-, 5'-bromo-2,4,5,7-tetrabromo-, 2,4,5,7-tetraiodo-, 5'-chloro-2,4,5,7-tetraiodo- and 5'-bromo-2,4,5,7-tetraiodonaphthalfluoresceins and also the corresponding sodium salts. The absorption maxima of the sodium salts of the dyes obtained were shifted towards the long-wave part of the spectrum in comparison with those of eosin and erythrosin.

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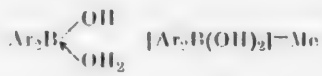
ORGANOBORON COMPOUNDS

XXXVI. UNSYMMETRICAL DIARYLBORIC ACIDS AND THEIR DERIVATIVES

B. M. Mikhailov and N. S. Fedotov

Institute of Organic Chemistry Academy of Sciences USSR

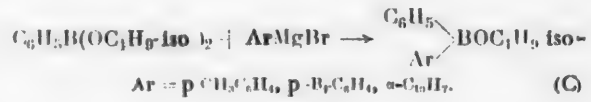
Certain of the known diarylboric acids exist in the form of complexes with water (A). Among these are the symmetrical acids, diphenylborenic and di-p-chlorophenylborenic [1], and the unsymmetrical ones, phenyl-o-tolylborenic and phenyl-p-chlorophenylborenic acids [2]. Di-p-bromophenylboric and di-α-naphthylboric acids do not contain water in the individual state, but in aqueous solutions they function as Lewis acids, reacting with bases to form the same type of salts (B) as acids existing in the hydrated form (A) in the individual state.



B

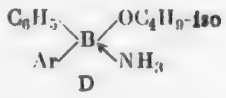
Continuing our study of complex formation among the aromatic compounds of boron, we undertook the synthesis of certain unsymmetrical diarylboric acids and their esters and acid chlorides and studied their complex-forming properties.

The isobutyl esters of unsymmetrical diarylboric acids (C) were synthesized by the action of appropriate Grignard reagents on the isobutyl ester of phenylboric acid.



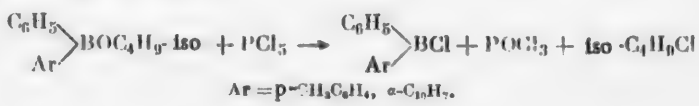
Ar = p-$CH_3C_6H_4$, p-$Br C_6H_4$, α-$C_{10}H_7$. (C)

The isobutyl esters of phenyl-p-tolylboric, phenyl-p-bromophenylboric and phenyl-α-naphthylboric acids were synthesized in this way. Like other diarylboric esters, [3] the esters obtained formed stable complexes (D) with ammonia.



D

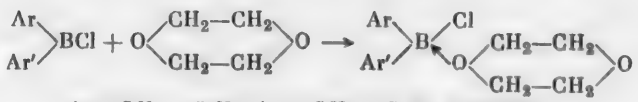
By the reaction with phosphorus pentachloride described previously [4], the isobutyl esters of phenyl-p-tolylboric and phenyl-α-naphthylboric acids were converted into the corresponding chlorides, phenyl-p-tolylboron and phenyl-α-naphthylboron chlorides.



Ar = p-$CH_3C_6H_4$, α-$C_{10}H_7$.

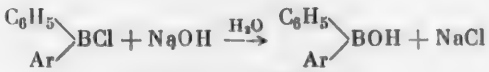
The reaction between phosphorus pentachloride and esters of phenyl-p-bromophenylboric acid proceeded anomalously and it was impossible to obtain phenyl-p-bromophenylboron chloride by this method.

The diarylboron chlorides were capable of forming solid complexes with dioxane in the ratio of 1 : 1. We prepared the dioxanates of phenyl-p-tolylboron and phenyl-α-naphthylboron chlorides and also of diphenylboron and di-α-naphthylboron chlorides, which we synthesized previously [4].



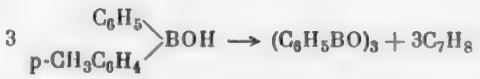
Ar = C_6H_5, α-$C_{10}H_7$; Ar′ = C_6H_5, α-$C_{10}H_7$, p-$CH_3C_6H_4$.

Hydrolysis of phenyl-α-naphthylboron and phenyl-p-tolylboron chlorides with an equimolecular amount of 1 N aqueous sodium hydroxide solution yielded phenyl-α-naphthylboric and phenyl-p-tolylboric acids, respectively, without any complex-bound water in their composition.



Ar = α-$C_{10}H_7$, p-$CH_3C_6H_4$.

Phenyl-p-tolylboric acid was extremely unstable and decomposed when stored for a short period into phenylboric anhydride and toluene.



Phenyl-α-naphthylboric acid was more stable, but we were unable to obtain phenyl-α-naphthylboric anhydride by the action of thionyl chloride in benzene solution on it, while the corresponding anhydrides are quite readily obtained from certain symmetrical acids by this method [5].

EXPERIMENTAL

All operations with organoboron compounds were carried out in a nitrogen atmosphere.

Isobutyl Phenyl-α-naphthylborate (I). Over a period of 1 hour, a solution of 88.3 g of isobutyl phenylborate [b.p. 125-127° (10 mm)] in 100 ml of absolute ether was added with stirring at -30-60° to a solution of 0.4 mole of α-naphthylmagnesium bromide in 600 ml of absolute ether. The reaction mixture was stirred for 6 hours at -60-70° and on the following day it was treated with 300 ml of 10% HCl. The ether was removed from the ether layer and combined ether extracts and the residue fractionated in vacuum. We obtained 80.8 g (80%) of (I) in the form of a thick, colorless oil with b.p. 207-208° (8 mm), d_4^{20} 1.0990, $n^{20}D$ 1.5970.

Found %: C 83.41; H 7.26; B 3.70. $C_{20}H_{21}OB$. Calculated %: C 83.31; H 7.34; B 3.75.

Ammoniate of Isobutyl Phenyl-α-naphthylborate (II). When dry ammonia was passed through a solution of 4.21 g of (I) in 50 ml of isopentane, a colorless, crystalline precipitate formed and this was collected and dried. We obtained 4 g (90%) of (II) with m.p. 90-92° (in a sealed capillary).

Found %: B 3.59. $C_{20}H_{24}ONB$. Calculated %: B 3.55.

Isobutyl Phenyl-p-tolylborate (III). Under the conditions of the previous experiment, the reaction of 0.5 mole of p-toluenemagnesium bromide and 93.5 g of isobutyl phenylborate yielded 41.6 g (41%) of (III) with b.p. 126-128° (1.5 mm), d_4^{20} 0.9720, $n^{20}D$ 1.5552.

Found %: C 81.30; H 8.42; B 4.09. $C_{17}H_{21}OB$. Calculated %: C 81.08; H 8.70; B 4.27.

Ammoniate of Isobutyl Phenyl-p-tolylborate (IV). Passing dry ammonia through a solution of 3.87 g of (III) in 50 ml of isopentane yielded 3.25 g (78%) of (IV) with m.p. 87-89° (in a sealed capillary).

Found %: B 4.60. $C_{17}H_{24}OB$. Calculated %: B 4.67.

Aminoethyl Ester of Phenyl-p-tolylboric Acid (V). To a solution of 1.76 g of (III) in 20 ml of 75% alcohol was added 0.84 g two fold excess) of monoethanolamine. The colorless crystalline precipitate was collected and dried. We obtained 1.45 g (87.3%) of (V) with m.p. 163-165°.

Found %: B 4.57. $C_{15}H_{16}ONB$. Calculated %: B 4.53.

Isobutyl Phenyl-p-bromophenylborate (VI). The reaction of 0.5 mole of p-bromophenylmagnesium bromide and 103 g of isobutyl phenylborate under the conditions described above yielded 52 g (33%) of (VI) with b.p. 152-153° (2 mm), d_4^{20} 1.9199, $n^{20}D$ 1.5773.

Found %: C 60.71; H 5.78; B 3.35. $C_{16}H_{18}OBBr$. Calculated %: C 60.60; H 5.68; B 3.41.

Phenyl-α-naphthylboron Chloride (VII). Into a Claisen flask was placed a solution of 13 g of (I) in 100 ml of absolute benzene and to it was added 9.4 g of phosphorus pentachloride in portions (after the addition of each portion of phosphorus pentachloride, the reaction mass heated up to 50-60°). When the whole of the phosphorus pentachloride had reacted, the isobutyl chloride, benzene and phosphorus oxychloride were distilled from the reaction mixture and the residue fractionated. We obtained 8.63 g (76.3%) of (VII) with b.p. 180-181° (4 mm); on standing, the substance crystallized as colorless needles with m.p. 87-90°.

Found %: C 77.06; H 4.99; B 4.35. $C_{16}H_{12}BCl$. Calculated %: C 76.68; H 4.82; B 4.31.

Phenyl-p-tolylboron Chloride (VIII). The reaction of 10 g of (III) and 8.5 g of phosphorus pentachloride under the conditions of the previous experiment (but without solvent and heating) yielded 4.2 g (50%) of (VIII) with b.p. 142-144° (8 mm), d_4^{20} 1.5783.

Found %: C 72.79; H 5.50; B 4.97; Cl 16.32. $C_{13}H_{12}BCl$. Calculated %: C 72.78; H 5.59; B 5.05; Cl 16.56.

Phenyl-α-naphthylboric Acid (IX). 2 g of (VII) was placed in a separatory funnel and dissolved in 20 ml of ether. To the ether solution obtained, cooled in ice-water, was added 8.1 ml of 1 N aqueous NaOH solution and the mixture shaken. The alkaline layer wasseparated and the ether layer dried over sodium sulfate for 2 hours. The ether was removed and the residue dried to constant loss in weight (0.002-0.003 g in 10 minutes) in vacuum at 1 mm. The liquid residue (1.78 g; 96% yield) was dissolved in 5 ml of isopentane and the solution cooled to -40°. The isopentane solution was decanted from the crystalline precipitate (the operation was carried out three times). The solvent was then removed in vacuum at room temperature. We obtained 0.87 g of (IX) as a thick, yellow liquid, which crystallized on standing; m.p. 57-59°.

Found %: C 82.97; H 5.95; B 4.53. $C_{16}H_{13}OB$. Calculated %: C 82.79; H 5.64; B 4.66.

Phenyl-p-tolylboric Acid (X). 2.9 g of (VIII), dissolved in 30 ml of ether, was hydrolyzed with 13.1 ml of 1 N aqueous NaOH solution under the conditions of the previous experiment. Removal of the ether and drying to a constant loss in weight (0.013-0.014 g in 10 minutes) in vacuum yielded 2.37 g (88%) of (X) as a colorless liquid.

Found %: C 79.45; H 6.69; B 5.28. $C_{13}H_{13}OB$. Calculated %: C 79.63; H 6.68; B 5.51.

The acid (X) was very unstable and even when stored for a short time it was converted into phenylboric anhydride. From 2.3 g of (X) we obtained 1.1 g (88%) of phenylboric anhydride, which had m.p. 212-214° after recrystallization from benzene and did not depress the melting point of an authentic sample.

Found %: Ar 72.92; B 10.07. C_6H_5OB. Calculated %: Ar 74.19; B 10.04.

Dioxanates of Diarylboron Chlorides

a) Dioxanate of Phenyl-p-tolylboron Chloride (XI). To 1 g of (VIII), placed in a two-necked flask, fitted with a calcium chloride tube and a dropping funnel, was added 2 ml of dioxane. The excess dioxane was distilled from the colorless, crystalline precipitate in vacuum and the crystals were washed with 10 ml of pentane, collected and dried. We obtained 0.7 g (50%) of (XI) with m.p. 72-76°.

Found %: B 3.70; Cl 11.53. $C_{17}H_{20}BO_2Cl$. Calculated %: B 3.57; Cl 11.74.

b) Dioxanate of Diphenylboron Chloride (XII). Under the same reaction conditions, 1.3 g of diphenylboron chloride yielded 1.3 g (70%) of (XII) with m.p. 80-85°.

Found %: B 3.72; Cl 11.92. $C_{16}H_{18}O_2BCl$. Calculated %: B 3.75; Cl 12.29.

c) Dioxanate of Di-α-naphthylboron Chloride (XIII). From 1.37 g of di-α-naphthylboron chloride (b.p. 216° at 2 mm) and 2 ml of dioxane we obtained 1 g (57%) of (XIII) with m.p. 93-96°.

Found %: B 2.84; Cl 8.64. $C_{24}H_{22}O_2BCl$. Calculated %: B 2.78; Cl 9.13.

d) Dioxanate of Phenyl-α-naphthylboron Chloride (XIV). 1.3 g of (VII) was mixed with an equimolecular amount of dioxane (0.45 ml) with heating. The viscous solution obtained was diluted with 1 ml of absolute ether and 1 ml of anhydrous isopentane. The colorless crystals precipitated were collected, washed with 10 ml of isopentane and dried. We obtained 0.7 g (40% of (XIV) with m.p. 90-91°.

Found %: B 3.22; Cl 10.03. $C_{20}H_{20}BO_2Cl$. Calculated %: B 3.19; Cl 10.48.

The chloride dioxanates were unstable and decomposed during storage.

SUMMARY

1. The isobutyl esters of phenyl-α-naphthylboric, phenyl-p-tolylboric and phenyl-p-bromophenylboric acids and phenyl-α-naphthylboron and phenyl-p-tolylboron chlorides were synthesized.

2. Phenyl-p-tolylboron, diphenylboron, di-α-naphthylboron and phenyl-α-naphthylboron chlorides formed complexes with dioxane (1 : 1).

3. On hydrolysis phenyl-α-naphthylboron and phenyl-p-tolylboron chlorides formed phenyl-α-naphthylboric and phenyl-p-tolylboric acids.

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ORGANOBORON COMPOUNDS

XXXVII. LITHIUM SALTS OF DIARYLBORIC ACIDS AND THEIR COMPLEXES WITH DIOXANE

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Investigations carried out in our laboratory showed that mono- and disubstituted organoboric acids reacted with bases like Lewis acids and did not form salts of the type $RB(OM)_2$ or R_2BOM but complex salts of mono- and disubstituted borenic acids $[RB(OH)_3]M$ or $[R_2B(OH)_2]M$ [1-3].

In the present work it was shown that in a nonaqueous medium diarylboric acids may react as protonic acids. We first encountered this interesting phenomenon in studying the reaction of phenyllithium with di-α-naphthylboric acid. It might have been expected that this would have given the stable lithium di-α-naphthylphenylborenate.

$$(\alpha\text{-}C_{10}H_7)_2BOH + C_6H_5Li \longrightarrow \left[(\alpha\text{-}C_{10}H_7)_2B\begin{matrix}C_6H_5\\OH\end{matrix}\right]Li$$

It was found, however, that the main reaction product was the lithium salt of di-α-naphthylboric acid $(\alpha\text{-}C_{10}H_7)_2BOLi$ (I). This salt was formed even more smoothly by treatment of di-α-naphthylboric acid with n-butyllithium in benzene solution.

$$(\alpha\text{-}C_{10}H_7)_2BOH + RLi \longrightarrow \underset{\substack{\text{(II)}\\ R = C_6H_5,\ n\text{-}C_4H_9.}}{\left[(\alpha\text{-}C_{10}H_7)_2B\begin{matrix}R\\OH\end{matrix}\right]Li} \longrightarrow \underset{\text{(I)}}{(\alpha\text{-}C_{10}H_7)_2BOLi} + RH$$

This is evidently connected with the fact that the initially formed borenic complexes (II) were unstable and decomposed in this case with the elimination of the radical that had formed part of the original organolithium compound.

The reaction between di-o-tolylboric acid and n-butyllithium was more complex and led to the formation of a mixture of lithium salts of di-o-tolylboric and o-tolylbutylboric acids. The formation of these salts is explained by the fact that in contrast to lithium di-α-naphthylbutylborenate (II), lithium di-o-tolylbutylborenate (III) decomposed in two ways losing butane and toluene.

$$(o\text{-}CH_3C_6H_4)_2BOH + n\text{-}C_4H_9Li \longrightarrow \underset{\text{(III)}}{\left[(o\text{-}CH_3C_6H_4)_2B\begin{matrix}C_4H_9\text{-}n\\OH\end{matrix}\right]Li}$$

$$\xrightarrow{-n\text{-}C_4H_{10}} (o\text{-}CH_3C_6H_4)_2BOLi \qquad \xrightarrow{-C_6H_5CH_3} (o\text{-}CH_3C_6H_4)(n\text{-}C_4H_9)BOLi$$

By treating the mixture of salts with dioxane in absolute ether we were able to isolate the main reaction product, the lithium salt of di-o-tolylboric acid, in a pure form as its complex with dioxane. The lithium salt of o-tolylbutylboric acid could not be isolated. Its presence in the mixture of reaction products was evident from the fact that determining the boron by an oxidation method [4] gave a much higher percentage boron content than determining it with mercuric chloride [5].

In order to avoid the side formation of salts of arylbutylboric acids, in subsequent experiments for the preparation of lithium salts of di-o-tolylboric and di-p-tolylboric acids we used not n-butyllithium but o-tolyl- or p-tolyllithium, respectively. The choice of the organolithium compounds was dictated by the fact that the elimination of one radical from lithium tri-o-tolyl- or tri-p-tolylborenate can only lead to the formation of the lithium salts of the corresponding diarylboric acids.

$$(o\text{-, p-}CH_3C_6H_4)_2BOH + o\text{-, p-}CH_3C_6H_4Li \longrightarrow [(o\text{-, p-}CH_3C_6H_4)_3BOH]Li \longrightarrow$$
$$\longrightarrow (o\text{-, p-}CH_3C_6H_4)_2BOLi + C_6H_5CH_3$$

The individual lithioaromatic compounds required were obtained by exchange reactions between aryl bromides and n-butyllithium in benzene-dioxane solution and isolated as their crystalline dioxanates [6]. p-Tolyllithium was also obtained from n-butyllithium and tri-p-tolylantimony [6].

In this way we obtained the lithium salt of di-p-tolylboric acid (from di-p-tolylboric acid and p-tolyllithium) and the dioxanate of the lithium salt of di-o-tolylboric acid (from di-o-tolylboric acid and o-tolyllithium dioxanate).

Interesting results which directly confirmed the general reaction scheme were obtained by studying the interaction of p-tolylboric acid and p-tolyllithium dioxanate in the presence of excess dioxane. The latter stabilized the initially formed lithium tri-p-tolylborenate to such an extent that it could be partly isolated from the reaction mixture as a complex with three molecules of dioxane (IV). Together with lithium tri-p-tolylborenate, we also isolated its conversion product, the lithium salt of di-p-tolylboric acid, as its dioxanate.

$$(p\text{-}CH_3C_6H_4)_2BOH + p\text{-}CH_3C_6H_4Li \cdot D + 2D \longrightarrow \underset{(IV)}{[(p\text{-}CH_3C_6H_4)_3BOH]Li \cdot 3D} \longrightarrow$$
$$\longrightarrow (n\text{-}CH_3C_6H_4)_2BOLi \cdot D + C_6H_5CH_3 + 2D$$
$$D = 1,4\text{-dioxane}$$

The dioxanates of lithium salts of diarylboric acids could also be obtained by the direct action of lithium reagents on the dioxanates of diarylboric acids. Thus, the dioxanate of di-α-naphthylboric acid and n-butyllithium yielded the dioxanate of lithium di-α-naphthylborate (V).

$$2(\alpha\text{-}C_{10}H_7)_2BOH + C_4H_8O_2 \longrightarrow 2(\alpha\text{-}C_{10}H_7)_2BOH \cdot C_4H_8O_2$$
$$2(\alpha\text{-}C_{10}H_7)_2BOH \cdot C_4H_8O_2 + 2n\text{-}C_4H_9Li \longrightarrow \underset{(V)}{2(\alpha\text{-}C_{10}H_7)_2BOLi \cdot C_4H_8O_2} + 2n\text{-}C_4H_{10}$$

The lithium salt of di-α-naphthylboric acid did not react with methyl iodide in boiling n-hexane but was methylated smoothly by dimethyl sulfate to form the methyl ester of di-α-naphthylboric acid.

$$(\alpha\text{-}C_{10}H_7)_2BOLi + (CH_3)_2SO_4 \longrightarrow (\alpha\text{-}C_{10}H_7)_2BOCH_3 + CH_3SO_4Li$$

Methanolysis of the lithium salt of di-α-naphthylboric acid proceeded, as was expected, according to the scheme

$$(\alpha\text{-}C_{10}H_7)_2BOLi + CH_3OH \longrightarrow \underset{(VI)}{\left[(\alpha\text{-}C_{10}H_7)_2B\begin{matrix}OCH_3\\OH\end{matrix}\right]Li}$$

When this reaction was carried out in an ether medium lithium di-α-naphthylmethoxyborenate (VI) was isolated in the form of its monoetherate.

EXPERIMENTAL

Di-o-tolyl- and di-p-tolylboric acids were obtained by hydrolysis of their aminoethyl esters. The latter were synthesized by the method described previously [7] from isobutyl metaborate and the appropriate organomagnesium compounds. Increasing the concentration of the o- and p-tolylmagnesium bromides to 2 moles per liter of ether made it possible to obtain the aminoethyl esters mentioned in 70-75% yields. When 1 molar solutions of Grignard reagents were used [7], the yields of aminoethyl ditolylborates did not exceed 40-42%.

All operations connected with preparing the lithium salts were carried out in an atmosphere of dry nitrogen. The aryl groups and boron were determined as usual by Wittig's method [5]; lithium was determined by titration with 0.1 N acid in aqueous or aqueous alcohol solution.

Lithium Salt of Di-α-naphthylboric Acid. Without cooling, a benzene solution containing 0.018 mole of n-butyllithium was added with shaking to a solution of 5 g of di-α-naphthylboric acid in 25 ml of anhydrous benzene. The reaction proceeded with noticeable heat evolution and the liberation of a finely crystalline, colorless precipitate. The reaction mixture was kept at room temperature for 10 hours and then the lithium salt was collected, washed with n-hexane and dried in vacuum. The yield was 4.45 g (87.3%).

Found %: C 82.95, 82.89; H 5.40, 5.40; B 3.49, 3.55; Li 2.33, 2.37. $C_{20}H_{14}OBLi$. Calculated %: C 83.38; H 4.90; B 3.75; Li 2.41.

The lithium salt of di-α-naphthylboric acid was sparingly soluble in benzene and ether, moderately soluble in methylene dichloride and insoluble in hexane.

Lithium Salt of Di-p-tolylboric Acid. 2.1 g of di-p-tolylboric acid was dissolved in 5 ml of absolute ether and mixed with shaking with an ether solution of 0.01 mole of p-tolyllithium, prepared from tri-p-tolylantimony and n-butyllithium [6]. The ether was removed at 100° (10 mm) and the residue kept for 5 minutes at 100° (3 mm) and then treated with 8 ml of anhydrous n-hexane. The colorless, crystalline reaction product was collected, washed with hexane (3 × 2 ml) and dried in vacuum.

Found %: $CH_3C_6H_4$ 83.98, 83.87; B 4.41, 4.58; Li 3.23, 3.20. $C_{14}H_{14}OBLi$. Calculated %: $CH_3C_6H_4$ 84.37; B 5.01; Li 3.21.

The yield of lithium di-p-tolylborate was 1.90 g (88%).

Dioxanate of Lithium Di-o-tolylborate. A. From Di-o-tolylboric Acid and N-butyllithium. With vigorous stirring, a benzene solution of 0.0238 mole of n-butyllithium was added to a warm solution of 5 g of di-o-tolylboric acid in 40 ml of anhydrous n-hexane. After the reaction mixture had been stirred for 2 hours at room temperature, the precipitate of salts was collected, washed with anhydrous n-hexane (2 × 10 ml) and dried to constant weight in vacuum. We obtained 4.32 g of substance.

Found %: B 5.70, 5.44 (oxid.); 4.70, 4.74 (det. with mercuric chloride); Li 3.41, 3.34. $C_{14}H_{14}BOLi$. Calculated %: B 5.01; Li 3.21. $C_{11}H_{16}BOLi$. Calculated %: B 5.95; Li 3.81.

The 2.47 g of salts obtained in this way was treated on a filter with a solution of 2.5 ml of dioxane in 25 ml of absolute ether and then extracted many times on the filter with boiling ether. For this purpose the lower joint of the filter funnel was attached to a flask with boiling solvent and the upper tube of the funnel was connected to a reflux condenser. The residue on the filter after treating the mixture of lithium salts in the manner described weighed 0.75 g. The ether – dioxane solution was evaporated to 10-15 ml in vacuum, mixed with 10 ml of anhydrous isopentane and kept at 0° for 12 hours. The precipitate was collected, washed with a 1:1 mixture of absolute ether and isopentane and recrystallized from 20 ml of absolute ether with 1 ml of anhydrous dioxane added. We obtained 1.90 g of the dioxanate of lithium di-o-tolylborate.

Found %: C 71.24, 70.96; H 7.29, 7.48; B 3.40, 3.45; Li 2.21, 2.23. $C_{18}H_{22}O_3BLi$. Calculated %: C 71.09; H 7.29; B 3.56; Li 2.28.

The dioxanate of lithium di-o-tolylborate was readily soluble in benzene, sparingly soluble in ether and insoluble in isopentane.

B. From Di-o-tolylboric Acid and o-Tolyllithium Dioxanate. Without cooling, a solution of 2.20 g of di-o-tolylboric acid in a mixture of 5 ml of absolute ether and 1 ml of anhydrous dioxane was added to a solution of 0.011 mole of o-tolyllithium dioxanate in 15 ml of absolute ether. The reaction proceeded with noticeable heat evolution and the liberation of a finely crystalline, colorless precipitate of the lithium salt. The reaction mixture was evaporated in vacuum to 1/3 of its original volume and left at 0° for 12 hours for further crystallization. The precipitate of the lithium salt dioxanate was collected, washed with 10 ml of a mixture of absolute ether and isopentane (1 : 1) and then isopentane (2 × 2.5 ml) and dried in vacuum. We obtained 1.8 g of substance. The filtrate was again evaporated in vacuum and the residue diluted with a mixture of 5 ml of isopentane and 2.5 ml of absolute ether to yield a further 0.66 g of dioxanate. The total yield of the dioxanate of lithium di-o-tolylborate was 2.46 g (77%).

The dioxanate of the lithium salt was recrystallized from absolute ether with dioxane added.

Found %: $CH_3C_6H_4$ 59.65, 59.79; B 3.44, 3.50; Li 2.23, 2.25. $C_{14}H_{14}OBLi \cdot C_4H_8O_2$. Calculated %: $CH_3C_6H_4$ 59.93; B 3.56; Li 2.28.

Dioxanate of Lithium Di-p-tolylborate. Dioxanate of Lithium Tri-p-tolylborenate. To a solution of 3.15 g of p-tolyllithium dioxanate in 40 ml of absolute ether was added 1 ml of dioxane and then a solution of 3.10 g of di-p-tolylboric acid in 10 ml of ether was introduced with shaking. The reaction mixture was evaporated to 10-15 ml, diluted with 5 ml of isopentane and kept at 0° for 12 hours. The precipitate of salts was collected, washed with 6 ml of a mixture of absolute ether and isopentane (1 : 5) and dried in vacuum. We obtained 3.2 g of salts. The reaction products were treated on a filter with a mixture of 20 ml of absolute ether and 2 ml of dioxane and then extracted many times with boiling ether. The undissolved residue weighed 1.4 g and was the dioxanate of lithium di-p-tolylborate.

Found %: $CH_3C_6H_4$ 61.80, 62.08; B 3.71, 3.69; Li 2.05, 2.10. $C_{14}H_{14}OBLi \cdot C_4H_8O_2$. Calculated %: $CH_3C_6H_4$ 59.93; B 3.56; Li 2.28.

The filtrate with a slight precipitate, liberated from the ether solution during the extraction, was evaporated in vacuum to approximately 10 ml, mixed with 5 ml of isopentane and kept at 0° for 6 hours. The finely crystalline, colorless precipitate of the dioxanate of lithium tri-p-tolylborenate (1.40 g) was collected, washed with isopentane (3 × 3 ml) and dried in vacuum.

Found %: $CH_3C_6H_4$ 49.39, 49.20; B 2.08, 2.03; Li 1.24, 1.20. $C_{21}H_{22}BOLi \cdot 3C_4H_8O_2$. Calculated %: $CH_3C_6H_4$ 47.76; B 1.89; Li 1.21.

Dioxanate of Di-α-naphthylboric Acid. To a solution of 2.82 g of di-α-naphthylboric acid in 10 ml of absolute ether was added a solution of 0.88 g of dioxane in 2.5 ml of ether. After 3-5 minutes, the solution began to deposit crystals of the dioxanate. The reaction product was collected, washed with a mixture (1 : 1) of absolute ether and isopentane (2 × 5 ml) and dried in vacuum. We obtained 3.00 g (92%) of the dioxanates of di-α-naphthylboric acid with m.p. 130-131°.

Found %: C 80.66, 80.77; H 5.98, 5.82; B 3.40, 3.35. $C_{44}H_{41}BO_3$. Calculated %: C 81.07; H 5.87; B 3.32.

Dioxanate of Lithium Di-α-naphthylborate. 2.90 g of the dioxanate of di-α-naphthylboric acid was dissolved in 20 ml of anhydrous benzene and treated at room temperature with a benzene solution of 0.009 mole of n-butyllithium. The reaction solution was evaporated at 80° (15 mm) and the residue mixed with 10 ml of absolute ether and 5 ml of a mixture (1 : 1) of absolute ether and n-hexane, filtered, washed with a mixture of absolute ether and n-hexane and dried in vacuum. The yield of the dioxanate of lithium di-α-naphthylborate was 2 g (69%).

Found %: $C_{10}H_7$ 73.53, 73.80; B 3.46, 3.40; Li 1.95, 1.98. $C_{40}H_{28}OBLi \cdot C_4H_8O_2$. Calculated %: $C_{10}H_7$ 76.57; B 3.26; Li 2.09.

Methyl Ester of Di-α-naphthylboric Acid. To a suspension of 1.6 g of the lithium salt of di-α-naphthylboric acid in 10 ml of anhydrous benzene was added 1.06 g of dimethyl sulfate. The reaction mixture was boiled for 2 hours. The benzene solution was cooled and freed from the finely crystalline precipitate of lithium methylsulfate (0.64 g) by filtration. The benzene filtrate was evaporated at 100° (10 mm) and the residue mixed with 3 ml of anhydrous methyl alcohol. We obtained 1.2 g (72.3%) of the methyl ester of di-α-naphthylboric acid with m.p. 95-98°. After recrystallization from n-hexane, the product had m.p. 101-103°.

Found %: C 85.06, 85.32; H 5.81, 5.83; B 3.63, 3.65. $C_{21}H_{17}OB$. Calculated %: C 85.16; H 5.78; B 3.65.

The substance was readily soluble in ether and benzene and sparingly soluble in methyl alcohol, n-hexane and isopentane.

Lithium Di-α-naphthylmethoxyborenate. A suspension of 1.50 g of lithium di-α-naphthylborate in 10 ml of absolute ether was treated with 0.17 g of anhydrous methyl alcohol. The reaction proceeded with slight heat evolution and solution of the original lithium salt in ether. After 15 minutes, the ether solution was filtered and evaporated at 50° (10 mm). The residue was mixed with 3 ml of anhydrous benzene and 3 ml of anhydrous hexane. The residue was collected, washed with anhydrous n-hexane (3 × 3 ml) and dried to constant weight in vacuum. We obtained 1.46 g (71%) of a complex corresponding in analysis to the monoetherate of lithium di-α-naphthylmethoxyborenate.

Found %: C 76.88, 76.73; H 6.76, 7.09; B 2.94, 2.90; Li 1.98, 1.91. $C_{24}H_{23}O_2BLi$. Calculated %: 76.16; H 7.16; B 2.74; Li 1.76.

SUMMARY

1. The interaction of diarylboric acids and aryllithiums or butyllithium formed unstable lithium triaryl- or diarylbutylborenates.

2. Lithium di-o-tolylbutylborenate decomposed losing butane and toluene to form a mixture of the lithium salts of di-o-tolylboric and o-tolylbutylboric acids.

3. Decomposition of the symmetrical lithium triarylborenates or lithium di-α-naphthylbutylborenate yielded the lithium salts of the corresponding diarylboric acids.

4. The lithium salts of diarylboric acids were isolated either in this form or as their complexes with dioxane.

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β-NAPHTHYL DERIVATIVES OF THE $ArPbX_3$ CLASS

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Previously one of us and M. M. Nad' [1] showed that organolead compounds of the Ar_2PbX_2 class (where Ar is an aromatic radical) were formed according to the equation

$$2Ar_2Hg + Pb(OOCCH_3)_4 \rightarrow Ar_2Pb(OOCCH_3)_2 + 2ArHgOOCCH_3$$

Among the compounds obtained in this was di-β-naphthyllead diacetate, which was the only organolead compound containing a β-naphthyl group described up to the present work.

We recently found [2] that the same starting reagents in molar ratios gave the compounds $ArPbX_3$, identical with the representatives of this class we obtained previously by another method [3]. It seemed interesting to synthesize the salts $\beta\text{-}C_{10}H_7Pb(OOCR)_3$, starting from di-β-naphthylmercury and to obtain fuller data on the β-naphthyl compounds of lead.

In the present work we synthesized β-naphthyllead triacetate, β-naphthyllead tripropionate and β-naphthylplumbonic acid. It was shown that the latter could serve as an intermediate in the replacement of one organic acid residue by another.

The compounds $ArPbX_3$ are the first stage in the arylation of tetravalent lead salts of organic acids by the equation presented above and should react with Ar_2Hg to form Ar_2PbX_2. Thus, the formation of Ar_2PbX_2 is accomplished in two stages. In actual fact β-naphthyllead triacetate reacted with di-β-naphthylmercury to give di-β-naphthyllead diacetate. An analogous reaction was observed by Criegee, Dimroth and Schempf* on the example of diphenyllead diacetate formation [4].

It should be noted that compounds of the $\beta\text{-}C_{10}H_7Pb(OOCR)_3$ series formed more slowly and crystallized with more difficulty than the corresponding derivatives of the α-naphthyl series which we described previously [5].

The acetates are convenient lead salts for the work: reactions with them proceeded smoothly, they were easier to isolate from the reaction mixture and the yield was usually higher than when the salts of other acids were used.

EXPERIMENTAL

β-Naphthyllead Triacetate. To a solution of 1.1 g of lead tetraacetate in 15 ml of dry chloroform, acidified with 2 drops of acetic acid was added 1 g of di-β-naphthylmercury in small portions and after 40 minutes, the latter had dissolved. The solution acquired a yellowish brown color. After an hour, an equivalent amount of an alcohol solution of hydrogen chloride was added to the solution. The precipitate which formed was a side product, β-naphthylmercury chloride, (0.65 g, 82%) which had m.p. 264-265°. According to literature data the m.p. is 266-267° [6]. After removal of the solvent, the dry residue was recrystallized from ethyl acetate with a drop of acetic acid added. We obtained 0.42 g (38%) of β-naphthyllead triacetate with m.p. 106°. After a second recrystallization, the product had m.p. 108-109°.

*In 1957 these authors described the reaction between diarylmercury and lead tetraacetate without mentioning the fact that we had already published this method of preparing $ArPbX_3$ in 1956 [2].

Found %: Pb 40.88, 40.25. $C_{16}H_{16}O_6Pb$. Calculated %: Pb 40.52.

The yellow crystalline substance dissolved very readily in chloroform and benzene in the cold, readily in methyl and ethyl alcohols and ethyl acetate and very sparingly in ether and hexane. It dissolved sparingly in ligroin in the cold and moderately on heating.

β-Naphthylplumbonic Acid. When an alcohol solution of β-naphthyllead triacetate was added to excess 5% aqueous ammonia, a yellowish precipitate formed and this was washed with water, alcohol and ether and dried to constant weight in a desiccator over calcium chloride. We obtained a pale yellow amorphous powder. The yield was 85%.

Found %: Pb 56.17, 56.13. $C_{10}H_9O_2Pb$. Calculated %: Pb 56.42.

In external appearance and properties, the substance was reminiscent of α-naphthylplumbonic acid we described previously [5]. When ground with organic acids it again gave the salt β-$C_{10}H_7Pb(OOCR)_3$ (see next experiment).

β-Naphthyllead Tripropionate from β-Naphthylplumbonic Acid. 0.3 g of β-naphthylplumbonic acid was carefully ground with the calculated amount (+10% excess) of propionic acid. The solution was left to crystallize in a desiccator over alkali. The solid substance obtained was recrystallized from ligroin (b.p. 95-100°). The m.p. was 84-85°. The substance was identical with the β-naphthyllead tripropionate obtained by the direct method (see next experiment).

β-Naphthyllead Tripropionate. To a solution of 1.25 g of lead tetrapropionate in 20 ml of chloroform, acidified with 2 drops of propionic acid, was added 1 g of di-β-naphthylmercury; the latter gradually dissolved.

As usual, after 2 hours the equivalent amount of an alcohol solution of hydrogen chloride was added to the slightly yellowish solution, which was then cooled to 0°. We obtained 0.76 g (95%) of β-naphthylmercury chloride. The filtrate was left in air (or better in a vacuum desiccator) until the solvent was removed completely. After recrystallization from benzene, the residue (1.3 g) had m.p. 84-85°. The yield was 0.75 g (61%). After a second recrystallization from the same solvent, the substance had the same melting point.

Found %: Pb 37.05, 37.41. $C_{19}H_{22}O_6Pb$. Calculated %: Pb 37.45.

β-Naphthyllead tripropionate was a slightly yellowish crystalline substance, which dissolved readily in acetone, ethyl acetate, chloroform and methyl and ethyl alcohols in the cold; it was sparingly soluble in ligroin in the cold and moderately so on heating; it was sparingly soluble in hexane and isopentane even on heating.

Di-β-naphthyllead Diacetate. To a solution of 0.4 g of β-naphthyllead triacetate in 15 ml of dry chloroform was added 0.35 g of di-β-naphthylmercury. The mixture was heated until the latter dissolved completely and then left for 3 days. The solution was filtered, the solvent removed almost to dryness on a water bath and the residue left in air until the solvent had disappeared completely. The crystalline residue was washed twice with hot acetone and once with 3 ml of anhydrous alcohol acidified with 2 drops of acetic acid. We obtained a product with m.p. 235-236°. According to literature data the melting point of di-β-naphthyllead diacetate is 236-236.5° [1].

Lead Tetrapropionate. Lead tetraacetate was dissolved in eight times its weight of propionic acid and the solution was evaporated in vacuum at 50-60° to approximately two thirds of the original volume. Cooling the residue with ice – water yielded needlelike crystals of lead tetrapropionate. The yield was 83% and the m.p. 129-131°. According to literature data the m.p. is 132° [7].

SUMMARY

1. β-Naphthyllead triacetate, β-naphthyllead tripropionate and β-naphthylplumbonic acid were synthesized for the first time.

2. It was shown that β-naphthyllead triacetate may be converted into di-β-naphthyllead diacetate by reaction with diaryl compounds of mercury.

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ESTERS OF URETHANPHOSPHORIC ACIDS

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The dimethyl ester of methylurethan-N-phosphoric acid, $CH_3OCONHPO(OCH_3)_2$ [1], was recently prepared and found to be an active systemic insecticide [2], which was almost completely nontoxic to warm-blooded animals and was called "Kiev-20-35 preparation" (later K-20-35).

It seemed interesting to study in more detail the chemical and physiological properties of compounds related to K-20-35 and to find simpler and more convenient methods of synthesizing K-20-35 and its analogs, which could serve as the basis for developing a scheme for factory production.

Previously K-20-35 was obtained [1, 3] by a quite complicated scheme consisting of four stages and including the use of metallic sodium and giving over-all yield of about 45%.

$$C_2H_5OCONH_2 \xrightarrow{+PCl_5} C_2H_5OCON{=}PCl_3 \xrightarrow{t^\circ} OCNPOCl_2 \xrightarrow{+CH_3OH}$$
$$\longrightarrow CH_3OCONHPOCl_2 \xrightarrow{+2CH_3ONa} CH_3OCONHPO(OCH_3)_2$$

It was possible to develop two new schemes for the synthesis of K-20-35, the first of which consisted of three stages with an over-all yield of about 76% and the second of two stages with an over-all yield of about 80%.

$$CH_3OCONH_2 \xrightarrow{+PCl_5} CH_3OCON{=}PCl_3 \xrightarrow{+H_2O} CH_3OCONHPOCl_2 \xrightarrow{+2CH_3OH} \longrightarrow CH_3OCONHPO(OCH_3)_2 \quad (I)$$

$$CH_3OCONH_2 \xrightarrow{+PCl_5} CH_3OCON{=}PCl_3 \xrightarrow{+3CH_3OH} \longrightarrow 2HCl + CH_3Cl + CH_3OCONHPO(OCH_3)_2 \quad (II)$$

Scheme (II) was more convenient for preparing K-20-35 in large amounts while scheme (I) was more convenient for synthesizing K-20-35 homologs. In the synthesis of K-20-35 by scheme (II), the second stage yielded a solution of K-20-35 in methanol containing 2 moles of hydrogen chloride and 1 mole of methyl chloride to each mole of K-20-35. If this solution was stored at room temperature for more than 3 hours the yield of K-20-35 fell considerably apparently due to hydrohalogenolysis of K-20-35. However, if the methyl alcohol was rapidly removed by distillation immediately after the reaction then the yield of K-20-35 also fell since the methanolysis of the methyl trichlorophosphazocarbonate was incomplete.

Of the esters of trichlorophosphazocarbonic acid of the type $ROCON{=}PCl_3$, up to now only the ethyl ester was known [3, 4] and this was obtained by scheme (III).

$$C_2H_5OCONH_2 + PCl_5 \longrightarrow 2HCl + C_2H_5OCON{=}PCl_3$$

The methyl, isopropyl, n-propyl, isobutyl and n-butyl esters of trichlorophosphazocarbonic acid were obtained in quantitative yields by the same scheme. Reaction (III) was accompanied by the absorption of large amount of heat and the temperature of the reaction mixture (for 0.1 mole) 5-10 minutes after the beginning of

TABLE 1

Esters of Trichlorophosphazocarbonic Acid of the Type ROCON = = PCl_3

R	Equivalent found after hydrolysis*	Empirical formula	Decomposition temperature	
			beginning	end
CH_3	4.97, 4.92	$C_2H_3O_2NPCl_3$	22°	65°
C_2H_5	5.03, 4.98	$C_3H_5O_2NPCl_3$	25	70
iso-C_3H_7	4.90, 4.99	$C_4H_7O_2NPCl_3$	37	80
n-C_3H_7	5.01, 4.95	$C_4H_7O_2NPCl_3$	46	86
iso-C_4H_9	4.83, 5.07	$C_5H_9O_2NPCl_3$	69	90
n-C_4H_9	4.90, 4.87	$C_5H_9O_2NPCl_3$	78	95

*Calculated equivalent after hydrolysis 5.00.

TABLE 2

Diacid Chlorides of Urethan-N-phosphoric Acids of the Type ROCONHPOCl$_2$

R	Equiv. after hydrolysis	Empirical formula*	Melting point
CH_3	3.87, 3.89	$C_2H_4O_3NPCl_2$	47—50°**
C_2H_5	3.77, 4.10	$C_3H_6O_3NPCl_2$	23—25**
iso-C_3H_7	3.97, 4.05	$C_4H_8O_3NPCl_2$	75—77**
n-C_3H_7	3.82, 3.87	$C_4H_8O_3NPCl_2$	49—50
iso-C_4H_9	3.76, 3.84	$C_5H_{10}O_3NPCl_2$	Liquid
n-C_4H_9	3.73, 3.82	$C_5H_{10}O_3NPCl_2$	Liquid
cis-C_6H_{11}	3.84, 3.91	$C_7H_{12}O_3NPCl_2$***	110—111°

*For all compounds the calculated equiv. after hydrolysis was 4.00.

**Cf. [1].

***Found %: Cl 27.51, 27.45. Calculated %: Cl 27.30.

the reaction fell to -25° for the methyl and ethyl esters of trichlorophosphazocarbonic acid and to -15° for the other esters (at an air temperature of +20°). In the absence of external heating, the reaction was complete (for 0.1 mole) in 1 hour. A considerable amount of hydrogen chloride (about 70%) remained dissolved in the trichlorophosphazocarbonic ester, but was readily removed in vacuum (5-10 mm) in a period of 30-40 minutes.

All the trichlorophosphazocarbonic esters were colorless liquids which decomposed quantitatively on heating according to the scheme:

$$ROCON{=}PCl_3 \longrightarrow RCl + OCNPOCl_2 \qquad (IV)$$

With an increase in the molecular weight of the alkyl, the decomposition point was raised. Esters with iso-alkyls decomposed at lower temperatures than esters with normal-alkyls. Table 1 gives the temperatures of the beginning and end of reaction (IV) at a heating rate of 0.7° per minute (thermometer bulb in liquid).

Reaction (IV) was accompanied by the evolution of heat and therefore with careless heating the decomposition of trichlorophosphazocarbonic esters, especially with large amounts, could occur explosively. Reaction (IV) could be carried out quite safely if methyl trichlorophosphazocarbonate was slowly added from a dropping funnel to an empty flask heated to 50-60° on a water bath. Under these conditions decomposition occurred immediately

TABLE 3

Urethan-N-phosphoric Esters of the Type ROCONHPO(OR')$_2$

R	R'	N found (in %)	Empirical formula	N calculated (in %)
CH_3	CH_3	7.67, 7.85	$C_4H_{10}O_5NP$*	7.65
CH_3	C_2H_5	7.10, 6.90	$C_6H_{14}O_5NP$	6.63
C_2H_5	CH_3	6.89, 6.98	$C_5H_{12}O_5NP$	7.10
C_2H_5	C_2H_5	5.98, 6.02	$C_7H_{16}O_5NP$	6.20
C_2H_5	n-C_3H_7	5.44, 5.32	$C_9H_{20}O_5NP$	5.53
C_2H_5	iso-C_3H_7	5.30, 5.50	$C_9H_{20}O_5NP$	5.53
C_2H_5	n-C_4H_9	4.80, 4.75	$C_{11}H_{24}O_5NP$	4.99
C_2H_5	iso-C_4H_9	5.11, 5.20	$C_{11}H_{24}O_5NP$	4.99
n-C_3H_7	CH_3	6.82, 6.85	$C_6H_{14}O_5NP$	6.63
n-C_3H_7	C_2H_5	5.81, 5.92	$C_8H_{18}O_5NP$	5.85
iso-C_3H_7	n-C_3H_7	5.10, 5.20	$C_{10}H_{22}O_5NP$	5.24
n-C_3H_7	iso-C_3H_7	5.20, 5.00	$C_{10}H_{22}O_5NP$	5.24
n-C_3H_7	n-C_4H_9	4.49, 4.51	$C_{12}H_{26}O_5NP$	4.74
iso-C_3H_7	CH_3	6.69, 6.81	$C_6H_{14}O_5NP$	6.63
iso-C_3H_7	C_2H_5	6.23, 6.17	$C_8H_{18}O_5NP$	5.85
n-C_4H_9	CH_3	6.29, 6.11	$C_7H_{16}O_5NP$	6.20
n-C_4H_9	C_2H_5	5.46, 5.60	$C_9H_{20}O_5NP$	5.53
n-C_4H_9	n-C_3H_7	4.80, 4.79	$C_{11}H_{24}O_5NP$	4.98
iso-C_4H_9	CH_3	6.41, 6.39	$C_7H_{16}O_5NP$	6.20
iso-C_4H_9	n-C_3H_7	4.70, 4.81	$C_{11}H_{24}O_5NP$	4.98
iso-C_4H_9	iso-C_3H_7	4.77, 4.80	$C_{11}H_{24}O_5NP$	4.98
cis-C_6H_{11}	CH_3	5.72, 5.68	$C_9H_{18}O_5NP$**	5.57

*M.p. 64-65°.

**M.p. 75-76°.

and the bulk of the diacid chloride of the isocyanatophosphoric acid remained in the flask while the part carried along by the methyl chloride could be readily condensed in a trap cooled to -80°.

Diacid chlorides of urethan-N-phosphoric acid were previously obtained [1, 3, 4] by the scheme

$$OCNPOCl_2 + ROH \longrightarrow ROCONHPOCl_2 \qquad (V)$$

Now they can be obtained in almost quantitative yields by the formolysis and hydrolysis of trichlorophosphazocarbonic esters (cf. [5]) by the scheme

$$ROCON{=}PCl_3 \xrightarrow[(\text{or } HCOOH)]{+H_2O} ROCONHPOCl_2 \qquad (VI)$$

For small amounts it was more convenient to use formolysis in benzene solution and for large amounts the hydrolysis was best carried out with the theoretical amount of water without solvent and with vigorous stirring and cooling.

Table 2 gives the diacid chlorides of urethan-N-phosphoric acids, which were obtained by formolysis of appropriate esters of trichlorophosphazocarbonic acids by scheme (VI) with the exception of the diacid chloride of cyclohexylurethan-N-phosphoric acid, which was obtained by the action of cyclohexanol on the diacid chloride of isocyanatophosphoric acid (cf. [1]). (See the experimental section for a description of the hydrolysis of trichlorophosphazocarbonic esters with water).

In paper [1] it was reported that "the action of isopropyl, n-butyl and isobutyl alcohols and then the corresponding alcoholates on the acid chloride of isocyanatophosphoric acid formed trialkyl phosphites as the main reaction products." This report is incorrect and caused by an experimental error. In fact the action of sodium alcoholates on the diacid chlorides of urethan-N-phosphoric acid gave 75-85% yields of urethanphosphoric esters

of the type ROCONHPO(OR')$_2$ (Table 3), which were colorless, uncrystallizable thick liquids (with the exception of crystalline K-20-35 and the dimethyl ester of cyclohexylurethan-N-phosphoric acid) that dissolved readily in water, acetone, benzene, alcohol, dioxane, ether and methanol, with more difficulty in carbon tetrachloride and were difficultly soluble in ligroin.

The urethanphosphoric esters were weak acids and could be titrated in alcohol solutions with aqueous 0.1 N sodium hydroxide solution in the presence of phenolphthalein to 0.75-0.80 equiv. Their crystalline sodium salts could be obtained by mixing equimolecular amounts of aqueous solutions of sodium hydroxide and urethanphosphoric esters and evaporating the mixture in vacuum at room temperature. The sodium salts were very readily soluble in water and their aqueous solutions showed an alkaline reaction to phenolphthalein. The structure of urethanphosphoric esters was confirmed by the fact that on thermal decomposition (cf. [6]) they gave alcohols and diesters of isocyanatophosphoric acids. If we started from the dimethyl esters of urethanphosphoric acids, then we obtained the corresponding alcohol and dimethyl ester of isocyanatophosphoric acid, which reacted with methanol quantitatively to give crystalline K-20-35, for example:

$$C_2H_5OCONHPO(OCH_3)_2 \xrightarrow{t^\circ} C_2H_5OH + OCNPO(OCH_3)_2;$$

$$OCNPO(OCH_3)_2 + CH_3OH \rightarrow CH_3OCONHPO(OCH_3)_2$$

The most active systemic insecticide of the urethanphosphoric esters was the dimethyl ester of isopropylurethan-N-phosphoric acid, whose activity was several times greater than that of K-20-35.*

EXPERIMENTAL

Preparation of K-20-35 by Scheme (I). Stage I. Preparation of Methyl Trichlorophosphazocarbonate. Into a weighed, two-liter, round-bottomed and three-necked flask fitted with a stirrer, thermometer and outlet tube attached to an HCl trap was placed 1 mole of powdered methyl urethan and 1 mole of powdered PCl_5; the mixture was shaken vigorously until it became a homogeneous, semiliquid mass (about 5 minutes). The stirrer was then started and 2 moles of methyl urethan and 2 moles of PCl_5 added. After 5 minutes another 2 moles of methyl urethan and another 2 moles of PCl_5 were added. At this, HCl was evolved vigorously and the temperature of the mixture fell to -25°. To accelerate the process, the flask was immersed in a water bath heated to 35-40° and then the heating controlled so that the temperature of the mixture was close to +5° (the thermometer bulb had to be immersed in the reaction mixture!) and did not exceed +10°. To accelerate the removal of HCl, a vacuum line was attached to the trap. After 40-45 minutes, the evolution of HCl slowed. The reaction was complete when all the lumps of PCl_5 and methyl urethan had dissolved completely (about 1 hour) and when the weight of the product was not more than 20 g above the weight of 5 moles of methyl trichlorophosphazocarbonate. At atmospheric pressure, methyl trichlorophosphazocarbonate retained a considerable amount of HCl (about 15% of its weight) in a dissolved state. The whole of the process required 1.5-2 hours.

Methyl trichlorophosphazocarbonate was a colorless liquid with a sharp odor and was similar to glycerol in appearance; it could be stored for many days in the absence of moisture at a temperature below 10°. At a temperature above 22° it decomposed violently to methyl chloride and the acid chloride of isocyanatophosphoric acid and this could lead to an explosion. Therefore, during the synthesis and storage the temperature of the substance was not allowed to rise above 10° and superheated spots were avoided. Vessels with methyl trichlorophosphazocarbonate were always kept in an ice bath, whose level had to be above the level of the substance in the vessel. The product could not be stored in cold cupboards (cooled with air) since this could readily lead to superheated spots. When these rules were obeyed strictly, the preparation of 5 moles of methyl trichlorophosphazocarbonate in one batch did not present any danger.

Other esters of trichlorophosphazocarbonic acid were prepared by this method in 0.1-1.0 mole amounts in one batch (see Table 1).

*According to the experiments of G. A. Efimov in the Insecticide Chemistry Laboratory of the Institute of Organic Chemistry of the Academy of Sciences, Ukrainian SSR.

Stage II. Preparation of Diacid Chloride of Methylurethan-N-phosphoric Acid. Into a weighed, three-necked, liter flask fitted with a stirrer, thermometer, dropping funnel and gas outlet tube with an HCl trap was placed 1 mole of methyl trichlorophosphazocarbonate, which was cooled to -10° (thermometer bulb in liquid). Then 1 mole of water was added slowly with vigorous stirring at such a rate that the temperature inside the flask did not exceed +5°. The reaction proceeded very vigorously at first with the evolution of a large amount of heat and more calmly at the end. When the whole of the water had been added, the reaction mixture rapidly crystallized completely. To remove the hydrogen chloride dissolved in the solid mass, the product was kept in vacuum for 30-40 minutes. The yield was quantitative and the m.p. 48-50°; the product did not depress the melting point of the diacid chloride of methylurethan-N-phosphoric acid obtained by the action of methanol on the diacid chloride of isocyanatophosphoric acid [1]. The product reacted slowly with atmospheric moisture and could be stored for several months without change in well-sealed bottles.

The diacid chlorides of other urethan-N-phosphoric acids could be obtained by the same method but it was more convenient to prepare them in small amounts by formolysis (see Table 2). For this, to 0.1 mole of the trichlorophosphazocarbonic ester was slowly added 0.105 mole of anhydrous formic acid with external cooling and vigorous stirring at such a rate that the temperature of the reaction mixture did not rise above 10°. The reaction proceeded violently at first but after the addition of one third of the acid it was smoother. The reaction product was kept in vacuum for 20-30 minutes to remove the HCl. The whole of the process required about 2 hours. The yields were about 90%. In some cases it was more convenient to carry out the reaction in benzene.

Stage III. Preparation of K-20-35. With stirring and cooling, 600 ml of methanol was added to a solution of 1 mole of the diacid chloride of methylurethan-N-phosphoric acid in 300 ml of benzene at such a rate that the temperature of the reaction mixture did not exceed +10°. It was also possible to add the solid diacid chloride of methylurethan-N-phosphoric acid in small portions with stirring to cooled methanol (600 ml) at such a rate that the temperature of the solution did not exceed +10°. Further processing of the solution was the same as in the preparation of K-20-35 by scheme (II). The yield was about 85%.

Preparation of K-20-35 by Scheme (II). Stage (I) was carried out as in the preparation by scheme (I).

Stage II. Into a 5-liter, three-necked, round-bottomed flask fitted with a stirrer, thermometer and dropping funnel was placed 3 liters of methanol and with vigorous stirring and cooling 5 moles of methyl trichlorophosphazocarbonate was added in 15-20 ml portions at such a rate that the temperature of the reaction mixture remained at about +5° (but not above +10°). The reaction proceeded violently with the strong evolution of heat. With efficient cooling [-15 – (-20°)] the addition of methyl trichlorophosphazocarbonate required 2-3 hours and then the reaction mixture was heated to 20° and left at room temperature with the precaution that the temperature in the liquid did not rise above 25°. After an hour the solution was evaporated in a water-pump vacuum with a receiver cooled to -15° and the solution on a water bath heated to 25°. The methyl alcohol condensed in the receiver and the methyl chloride passed into the pump. After 30 minutes, when the methyl chloride had been removed completely, the evaporation was continued in an oil-pump vacuum (at a pressure of not more than 15 mm) with the receiver cooled to -15°. The air in the capillary was passed through a column with P_2O_5. Methanol containing 4-5% HCl distilled at first and then the concentration of HCl in the methanol distilled gradually increased. The distillation of the methyl chloride, methanol and hydrogen chloride should be completed in 3-4 hours. If the distillation required a longer time then the yield was noticeably reduced. With a vacuum of 15 mm, the temperature of the water bath could be raised to 40° at first, but toward the end of the distillation the temperature of the bath had to be no higher than 30°. If the distillation could not be completed in 3-4 hours in one flask, then the solution was divided into 3-4 portions and evaporated simultaneously in 3-4 flasks. The methanol distillates containing HCl, were recovered by rectification, then neutralized with a methanol solution of ammonia, the NH_4Cl removed by filtration and the methanol distilled. When the evaporation was complete, the colorless, sirupy residue gradually changed into a solid crystalline mass, which was dissolved in 500 ml of methanol and a 15% methanol solution of ammonia added to the solution until the acid reaction to congo disappeared. The more carefully the evaporation was carried out, the smaller the amount of HCl and acid side-products that remained in solution, the less the ammonia required for their neutralization and the higher the yield. It was satisfactory if 150 ml of 15% NH_3 in methanol was required for the neutralization. Excess ammonia had to be avoided as it reacted with K-20-35.

The neutralized solution was evaporated in vacuum (15 mm, bath temperature 30-40° and receiver temperature -15°) and the crystalline residue (yield about 95%, m.p. 66-71° – the melt was not clear and contained

about 15% of impurities) was treated with 2 liters of dichloroethane in which K-20-35 was readily soluble and the side products (after neutralization with ammonia) were insoluble. The residue was removed by filtration and washed with dichloroethane and the filtrate evaporated in vacuum at 30-40°. The residue was K-20-35 in about 80% yield and had m.p. 63-64° (clear melt).

Thermal Decomposition of Trichlorophosphazocarbonic Esters. 0.1 mole of methyl trichlorophosphazocarbonate was heated at a rate of 0.6-0.7° per minute in a round-bottomed flask connected to a trap cooled to -75°. We obtained about 90% of methyl chloride (b.p. -22 to -23°) and 96% of the diacid chloride of isocyanatophosphoric acid (b.p. 45-46° at 20 mm). The other esters were decomposed in the same way (Table 1).

Preparation of Urethan-N-phosphoric Esters From the Diacid Chlorides of Urethan-N-phosphoric Acids and Alcoholates. A solution of 0.1 mole of the diacid chloride of urethan-N-phosphoric acid in 30 ml of benzene was added with vigorous stirring and cooling to a solution of 0.2 mole of sodium alcoholate in 2 mole of the corresponding alcohol at such a rate that the temperature of the reaction mixture did not exceed +10°. The reaction proceeded vigorously and a precipitate of NaCl formed. Stirring was continued for 2-3 hours at room temperature, the solvent removed in vacuum at 30-40°, the residue treated with 100-150 ml of benzene, the NaCl removed by filtration and the filtrate evaporated in vacuum at 30-40°. Esters of urethan-N-phosphoric acids remained (Table 3).

Thermal decomposition of dimethyl ethylurethan-N-phosphoric acid was carried out under the conditions described previously [6]. The yield of dimethyl isocyanatophosphate was about 80%. The product was identified by conversion to K-20-35 by the action of methanol.

SUMMARY

1. The dimethyl ester of methylurethan-N-phosphoric acid (preparation "Kiev-20-35") was obtained directly from methyl trichlorophosphazocarbonate (in about 80% yield) and through the diacid chloride of methylurethan-N-phosphoric acid (in about 76% yield).

2. Some esters of trichlorophosphazocarbonic acid were prepared and a method was developed for converting them to the diacid chlorides of urethan-N-phosphoric acids by the action of water.

3. The temperature of the thermal decomposition of trichlorophosphazocarbonic esters to alkyl halides and diacid chlorides of isocyanatophosphoric acid depended on the nature of the alkyl. With an increase in the molecular weight of the alkyl the decomposition temperature increased. Esters with iso-alkyls decomposed at lower temperatures than their isomers with normal-alkyls.

4. A series of urethan-N-phosphoric esters was prepared and some of them were found to be active systemic insecticides, which were not toxic to warm-blooded animals.

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REACTION OF PHOSPHORUS PENTACHLORIDE WITH DIACID CHLORIDES AND DIESTERS OF ARYLSULFONAMIDOPHOSPHORIC ACIDS

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By the action of water or formic acid, alkyl and aryl trichlorophosphazosulfones of the type $RSO_2N=PCl_3$ are readily converted into diacid chlorides of the corresponding alkyl- and arylsulfonamidophosphoric acids [1] by the scheme

$$RSO_2N=PCl_3 + H_2O \longrightarrow HCl + RSO_2NHPOCl_2$$

It seemed interesting to determine whether it was possible to accomplish the reverse conversion, i.e.,to obtain the corresponding trichlorophosphazo compounds from the diacid chlorides of arylsulfonamidophosphoric acids:

$$RSO_2NHPOCl_2 + PCl_5 \longrightarrow HCl + POCl_3 + RSO_2N=PCl_3 \quad (I)$$

Experiments showed that reaction (I) proceeded readily with diacid chlorides of o-, m- and p-nitrophenylsulfonamidophosphoric acids at 130-135° for 10-15 minutes with yields of from 47 to 80% and for the phenyl ester of the N-(dichlorophosphinyl)-monoamide of p-benzenedisulfonic acid at 115-120° for 20-25 minutes with 49% yield. The reaction proceeded somewhat more slowly in carbon tetrachloride solution at the boiling point. In all cases the reaction was accompanied by the formation of side products which were pale yellow, uncrystallizable liquids, whose nature has not been determined as yet. The reaction of phosphorus pentachloride with the potassium salts of the diacid chlorides of nitrophenylsulfonamidophosphoric acids proceeded with approximately the same yields.

The corresponding trichlorophosphazo compounds were not formed by the action of phosphorus pentachloride on the diacid chlorides of phenyl-o-,and p-tolyl- and p-chlorophenylsulfonamidophosphoric acids. Thus, reaction (I) apparently proceeds only for diacid chlorides of arylsulfonamidophosphoric acids with second order substituents in the nucleus regardless of their position with respect to the $SO_2NHPOCl_2$ group. Judging by the yields of nitrophenyl trichlorophosphazosulfones (ortho 81, meta 47 and para 57%), the effect of a substituent of the second order, which promotes reaction (I), is transmitted by electromeric and inductive means (cf. [2]).

Diphenyl esters of arylsulfonamidophosphoric acids reacted with phosphorus pentachloride readily and in good yield regardless of the nature of the substituents in the aromatic nucleus and formed the corresponding aryl diphenoxychlorophosphazosulfones by the scheme

$$ArSO_2NHP(O)(OC_6H_5)_2 + PCl_5 \longrightarrow HCl + POCl_3 + ArSO_2N=PCl(OC_6H_5)_2$$

The aryl diphenoxychlorophosphazosulfones were low-melting, colorless, crystalline substances (cf. [3]), which dissolved readily in benzene, acetone and dioxane, with more difficulty in carbon tetrachloride and were insoluble in ligroin. The aryl diphenoxychlorophosphazosulfones were insoluble in ether with the exception of

Aryl Diphenoxychlorophosphazosulfones of the Type $(C_6H_5O)_2ClP{=}NSO_2Ar$

Substance No.	Ar	Yield (in %)	Melting point	Appearance; crystal. solvent	Found		Empirical formula	Cl calculated (in %)**
					% Cl	equivalent after hydrolysis		
(II)	C_6H_5	51	71—73°	Prisms; benzene + ligroin	see [4] 7.95, 7.90*	see [4] 2.02, 2.03	$C_{18}H_{14}O_4NCl_2SP$	8.03
	$p\text{-}ClC_6H_4$	77	91—93					
	$o\text{-}NO_2C_6H_4$	84	64—65	Needles; CCl_4 + ligroin	7.50, 7.66	1.98, 2.03	$C_{18}H_{14}O_6N_2ClSP$	7.84
(III)	$m\text{-}NO_2C_6H_4$	80	82—84	Needles; benzene + ether	7.71, 7.54	1.97, 2.00	$C_{18}H_{14}O_6N_2ClSP$	7.84
	$p\text{-}NO_2C_6H_4$	91	79—81	Needles; benzene + ligroin	7.61, 7.75	2.01, 2.03	$C_{18}H_{14}O_6N_2ClSP$	7.84

*Hydrolyzable chlorine.

**For all substances the calculated equivalent after hydrolysis equalled 2.

(III). The yields, melting points, external appearance and analytical data of the aryl diphenoxychlorophosphazosulfones are given in the table.

Aryl diphenoxychlorophosphazosulfones were slowly hydrolyzed by water with the formation of diphenyl esters of arylsulfonamidophosphoric acids. In the presence of phenolphthalein they titrated to two equivalents. The structure of the aryl diphenoxychlorophosphazosulfones was proved strictly by the fact that they could be converted in high yields into the corresponding aryl triphenoxyphosphazosulfones, which were identified by mixed melting points. In addition, (II) was found to be identical with phenyl diphenoxychlorophosphazosulfone, which was obtained previously by the action of the sodium salt of the N-chloroamide of benzenesulfonic acid on the acid chloride of diphenyl phosphite [4].

The phenyl ester of the N-(dichlorophosphinyl-(monoamide of p-benzenedisulfonic acid was obtained by the action of formic acid (cf. [1]) on the phenyl ester of p-trichlorophosphazosulfonobenzenesulfonic acid, which was synthesized by the action of phosphorus pentachloride on the phenyl ester of the monoamide of p-benzenedisulfonic acid; the latter was obtained by the action of sodium phenolate on the recently described monoacid chloride of the monoamide of p-benzenedisulfonic acid [5].

EXPERIMENTAL

Reaction of Phosphorus Pentachloride on the Diacid Chlorides of Nitroarylsulfonamidophosphoric Acids. A mixture of 0.03 mole of the diacid chloride of the nitroarylsulfonamidophosphoric acid, 0.0315 mole of PCl_5 and 5 ml of CCl_4 was boiled under reflux on an oil bath until the evolution of HCl ceased (30-40 minutes). The solvent, $POCl_3$ and excess PCl_5 were removed in vacuum at 80-90°. The residue was a clear, pale yellow liquid, which partially crystallized on cooling. The side product was a light yellow liquid, which was readily separated from the crystalline nitrophenyl trichlorophosphazosulfones by washing with a small amount of ether. Yields: o-nitrophenyl trichlorophosphazosulfone 81%, m.p. 69-71°; m-isomer 47%, m.p. 72-73°; p-isomer 57%, m.p. 115-117°. The products were identified by mixed melting points with authentic nitrophenyl trichlorophosphazosulfones [6].

The reaction could be carried out without solvent. In this case the mixture of diacid chloride of nitroarylsulfonamidophosphoric acid and PCl_5 was heated on an oil bath at 130-135° until the evolution of HCl ceased (10-15 minutes). The subsequent processing and yields were the same.

Reaction of Potassium Salt of Diacid Chloride of p-Nitrophenylsulfonamidophosphoric Acid With Phosphorus Pentachloride. A mixture of 0.02 mole of the potassium salt of the diacid chloride of p-nitrophenylsulfonamidophosphoric acid [7] and 0.021 mole of PCl_5 was heated on an oil bath at 130-135° until the evolution of HCl ceased (15-20 minutes), the $POCl_3$ removed in vacuum at 80°, the residue treated with benzene, the NaCl removed by filtration and the benzene removed in vacuum at 50°. The residue was a clear, light yellow liquid, which crystallized on cooling. The side-reaction products were washed out with a small amount of ether. The yield of p-nitrophenyl trichlorophosphazosulfone was 57% and the m.p. 115-117°. The product was identified by a mixed melting point.

Reaction of Phosphorus Pentachloride With the Phenyl Ester of the N-(dichlorophosphinyl)-monoamide of p-Benzenedisulfonic Acid. A mixture of 0.011 mole of PCl_5 and 0.01 mole of the phenyl ester of the N-(dichlorophosphinyl)-monoamide of p-benzenedisulfonic acid was heated on an oil bath at 115-120° until the evolution of HCl ceased and this required 20-25 minutes. The excess PCl_5 and $POCl_3$ were removed in vacuum at 60-70°. The residue was a light yellow, viscous liquid, which slowly crystallized when seeded and changed into a semisolid mixture of colorless crystals and a yellow oil. To remove the oily side products 5 ml of CCl_4 was added, the mixture stirred carefully and the crystalline phenyl ester of p-trichlorophosphazosulfonobenzenesulfonic acid collected and washed with 5 ml of CCl_4. The yield was 49% and the m.p. 103-104° and the product was identified by a mixed melting point.

Phenyl Ester of the Monoamide of p-Benzenedisulfonic Acid. With vigorous stirring, 0.1 mole of finely powdered sodium phenolate was added slowly to a solution of 0.1 mole of the monoacid chloride of the monoamide of p-benzenedisulfonic acid [5] in 50 ml of dioxane. The mixture gave off heat, the sodium phenolate dissolved and sodium chloride precipitated. After a day the mixture was heated for 1 hour on a boiling water bath, cooled and 200 ml of water added to the thick paste formed. The precipitate was collected, washed with water, dried in air and recrystallized from alcohol. The phenyl ester of the monoamide of p-benzenedisulfonic acid formed colorless needles with m.p. 173-174° and the yield was 61%; it was insoluble in water, dissolved in alcohol on heating, with more difficulty in benzene and was difficultly soluble in ether.

Found %: S 20.73, 20.81. $C_{12}H_{11}O_5NS_2$. Calculated %: S 20.47.

Phenyl Ester of p-Trichlorophosphazosulfonobenzenesulfonic Acid. A mixture of 0.03 mole of the phenyl ester of the monoamide of p-benzenedisulfonic acid and 0.033 mole of PCl_5 was heated on an oil bath. At 120° the reaction was complete in 30 minutes. The yield of the crude product was quantitative. The phenyl ester of p-trichlorophosphazosulfonobenzenesulfonic acid was a colorless, crystalline substance with m.p. 103-104°, which dissolved readily in ether and benzene and crystallized from CCl_4 as prisms.

Found: equiv. after hydrolysis 4.94, 4.89. $C_{12}H_9O_5NS_2PCl_3$. Calculated: equiv. after hydrolysis 5.00.

Phenyl Ester of N-(dichlorophosphinyl)-monoamide of p-Benzenedisulfonic Acid. To a solution of 0.02 mole of the phenyl ester of p-trichlorophosphazosulfonobenzenesulfonic acid in 15 ml of benzene was added 0.02 mole of formic acid. After 4 hours the reaction product was collected, washed with benzene and dried in vacuum. The yield was 84% and the m.p. 158-160°; the product formed fine, colorless platelets (from benzene), which dissolved readily in ether, with more difficulty in $CHCl_3$ and were difficultly soluble in C_6H_6, CCl_4 and ligroin.

Found: equiv. after hydrolysis 3.97, 4.03. $C_{12}H_{10}O_6NS_2PCl_2$. Calculated: equiv. after hydrolysis 4.00.

Preparation of Aryl Diphenoxychlorophosphazosulfones by the Action of Phosphorus Pentachloride on the Diphenyl Esters of Arylsulfonamidophosphoric Acids. 0.02 mole of the diphenyl ester of arylsulfonamidophosphoric acid and 0.02 mole of PCl_5 were heated on an oil bath at 100-110° until the evolution of HCl ceased (30-40 minutes). The phosphorus oxychloride formed was removed in vacuum. The residue was a yellow oil which crystallized on cooling. The crystalline mass was ground with a small amount of ether. At this, the yellow oily impurities dissolved. The crystalline residue was collected and washed with ether. (III), which was readily soluble in ether, was washed with ligroin. The final purification was by recrystallization (see table).

Conversion of Aryl Diphenoxychlorophosphazosulfones Into Aryl Triphenoxyphosphazosulfones. A mixture of 0.01 mole of aryl diphenoxychlorophosphazosulfone, 20 ml of benzene and 0.01 mole of sodium phenolate was boiled for 5 minutes and then the benzene removed in vacuum at 50°, the residue treated with water and the crystalline aryl triphenoxyphosphazosulfone collected, washed and recrystallized.

In this way we obtained: phenyl triphenoxyphosphazosulfone, 87% yield, m.p. 85-86° [3]; p-chlorophenyl derivative, yield 78%, m.p. 77-79°; o-nitrophenyl derivative, yield 96%, m.p. 78-79°; m-nitrophenyl derivative, yield 98%, m.p. 102-104° [6]. The products were identified by mixed melting points with authentic materials. The p-chlorophenyl derivatives have not been described in the literature and therefore they were synthesized by the scheme found previously [3].

p-Chlorophenyl Triphenoxyphosphazosulfone. With vigorous stirring 0.06 mole of sodium phenolate was added to a solution of 0.02 mole of p-chlorophenyl trichlorophosphazosulfone in 40 ml of benzene. The reaction proceeded with the evolution of heat. After several hours the reaction mixture was treated with water, the benzene layer separated and dried with sodium sulfate and the benzene removed by distillation. The residue was an oily liquid, which rapidly crystallized. p-Chlorophenyl triphenoxyphosphazosulfone formed colorless prisms (from a mixture of benzene and ligroin) with m.p. 78-80° in 87% yield. The product was soluble in alcohol, ether and benzene and difficultly soluble in ligroin.

Found %: Cl 7.29, 7.40. $C_{24}H_{19}O_5NClSP$. Calculated %: Cl 7.10.

Diphenyl Ester of p-Chlorophenylsulfonamidophosphoric Acid. With vigorous stirring 0.3 mole of sodium phenolate was gradually added to a solution of 0.1 mole of the diacid chloride of p-chlorophenylsulfonamidophosphoric acid in 50 ml of dioxane at such a rate that the reaction mixture boiled gently. Dioxane was removed in vacuum and residue treated with water. The difficultly water-soluble sodium salt of the diester was collected, suspended in water and decomposed by the addition of 20 ml of 5 N HCl. After 10-15 minutes the precipitate was collected, washed with water, dried and recrystallized. The diphenyl ester of p-chlorophenylsulfonamidophosphoric acid formed colorless platelets (from alcohol) with m.p. 168-170° in 90% yield. It was soluble in acetone, hot alcohol and benzene and insoluble in ligroin, CCl_4 and ether.

Found %: Cl 8.35, 8.38. $C_{18}H_{15}O_5NClSP$. Calculated %: Cl 8.38.

SUMMARY

1. The action of phosphorus pentachloride on the diacid chlorides of o-, m- and p-nitrophenylsulfonamidophosphoric acids and the phenyl ester of the N-(dichlorophosphinyl)-monoamide of p-benzenedisulfonic acid yielded the corresponding trichlorophosphazo compounds.

2. The corresponding aryl trichlorophosphazosulfones were not formed by the action of phosphorus pentachloride on the diacid chlorides of arylsulfonamidophosphoric acids whose molecules did not contain substituents of the second order in the aromatic nucleus.

3. The action of phosphorus pentachloride on the diphenyl esters of arylsulfonamidophosphoric acids yielded aryl diphenoxychlorophosphazosulfones regardless of the nature and the position of the substituents in the aromatic ring of the sulfonic acid.

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INVESTIGATION IN THE FIELD OF TRIAZINE DERIVATIVES

I. SOME SUBSTANTIVE TRIAZINE AZO DYES

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In 1922-1923 [1] the capacity of 2,4,6-trihalotriazines, in particular cyanuric chloride, to undergo stepwise replacement of the halogen atoms by residues from primary and secondary amines and aminoazo compounds was discovered. Due to this cyanuric chloride became widely used in the synthesis of various classes of dyes and in the case of direct azo dyes, it was used as a "chromophoric block" for connecting identical or different aminoazo compounds [2]. When two azo dyes are connected by a triazine ring into one molecule a single chromophoric system is not produced; the isolated chromophoric systems forming the one molecule show additivity in light-absorption phenomena. Due to this it became possible to synthesize substantive green azo dyes, which were obtainable by stepwise condensation of cyanuric chloride with yellow and blue aminoazo compounds [3]. It is possible to use other triazine derivatives, in particular methyl- and phenyldichlorotriazines, as "chromophoric blocks" in the synthesis of such dyes [4]. There are no data in the literature on the use of o- and p-methoxy- and o-hydroxyphenyldichlorotriazines in the synthesis of azo dyes.

It seemed interesting to us to syntheses triazine green azo dyes formed from the same blue and yellow components but differing in the nature of the third, colorless component attached to the triazine ring and to follow the effect of the latter on the color of the dyes obtained. It was to be expected that the nature of the colorless component would not affect the color of the whole system (in the visible region of the spectrum) if the triazine ring completely isolated the chromophoric systems attached to it. Incidentally, it was also interesting to follow the effect of the nature of substituents in the triazine ring on the lability of the halogens attached to it.

To elucidate the problems given, we synthesized green azo dyes based on cyanuric chloride (with one chlorine atom replaced by an aniline residue), 2-phenyl-4,6-dichloro-1,3,5-triazine and derivatives of the latter with o- and p-methoxy and o-hydroxy substituents in the phenyl nucleus. In all cases the blue component used was the aminodisazo dye of the composition (H-acid $\rightarrow$ cresidine $\xrightarrow{\text{alkali}}$ H-acid) and the yellow component was p-aminobenzeneazosalicylic acid.

The cyanuric dye (I) was obtained normally [5] by condensation of cyanuric chloride with the blue component, then with the yellow and finally with aniline. The other dyes (II) – (V) were obtained by condensing the aminoazo compounds with phenyldichlorotriazine and p- and o-methoxy- and o-hydroxyphenyldichlorotriazines, respectively. The dyes investigated were purified as their sodium salts by reprecipitation with sodium chloride from a dilute aqueous solution at 80° and their individuality was established chromatographically (the presence of sodium chloride was permissible); the dye content of the substance was determined by reduction with vanadium sulfate.

The starting phenyldichlorotriazine and its p- and o-methoxy derivatives were obtained according to literature data [6] according to the scheme: dicyandiamide $\rightarrow$ aroyldicyandiamide $\rightarrow$ aroylbiuret $\rightarrow$ aryldihydroxytriazine $\rightarrow$ aryldichlorotriazine. o-Hydroxyphenyldichlorotriazine was obtained by hydrolysis of o-methoxyphenyldichlorotriazine with hydrogen bromide and subsequent replacement of the bromine attached to the triazine ring by chlorine by the action of hydrogen chloride [7].

TABLE 1•

Dye	$\lambda_{max.}$ (mμ)	ε · 10⁻⁴	$\lambda_{max.}$ (mμ)	ε · 10⁻⁴
(I)	385	4.8	610	4.2
(II)	395	4.8	620	4.1
(III)		4.7		4.4
(IV)		4.6		4.3
(V)		4.8		4.3

•The accuracy with which the optical density was determined was ±3%.

TABLE 2

Dye	Duration of reaction (in hours)	
	stage 1	stage 2
(II)	24	30
(III)	26	34
(IV)	32	40
(V)	46	54

To determine the effect of the composition of the dyes investigated on their color, their aqueous solutions were examined spectrophotometrically at pH 6-6.5 and a molar concentration close to $2.5 \cdot 10^{-5}$. The results of the experiments are illustrated by the data presented in Table 1.

The data presented show that dyes with a phenyl directly attached to the triazine ring show a light-absorption maximum in a somewhat deeper region of the spectrum than dyes with the phenyl attached to the triazine through an imino group; the molar extinctions of the dyes were similar. Methoxy and hydroxy groups in the ortho- or para-positions of the phenyl nucleus directly attached to the triazine ring had no noticeable effect on the color.•

During the synthesis of dyes (II), (III), (IV) and (V) it was noted that the condensation of the aminoazo compounds used with the p- and o-methoxy derivatives of phenyldichlorotriazine proceeded somewhat more slowly than with the latter; the o-hydroxy derivative reacted considerably more slowly. The data obtained (see Table 2) led to the conclusion that in aryldichlorotriazines the lability of the chlorine atoms depended on the nature of the substituents in the ortho- or para-positions of the phenyl; nucleophilic substituents suppressed it.

EXPERIMENTAL

2-Phenyl-4,6-dichloro-1,3,5-triazine was synthesized from dicyandiamide by the scheme presented above. Benzoylation of dicyandiamide, conversion of benzoyldicyandiamide into benzoylbiuret and cyclization of the latter into phenyldihydroxytriazine were carried out under the conditions of paper [9]. When dicyandiamide was reacted with benzoyl chloride in a dioxane – water medium [10] with the other conditions the same as in the benzoylation in an aqueous acetone medium, a lower yield was obtained; the benzoylation product could not be isolated with cellosolve – water and acetone – water media. The hydroxyl in phenyldihydroxytriazine was replaced by chlorine by reaction with phosphorus pentachloride in phosphorus oxychloride [6], phosphorus trichloride, thionyl chloride or chlorobenzene and with phosphorus trichloride and chlorine in chlorobenzene.

Into a boiling mixture (reflux condenser) of 13 g of phenyldihydroxytriazine (beginning to melt at 273°), 20.8 g of phosphorus trichloride and 45 ml of chlorobenzene was passed dry chlorine until the suspension changed to a solution and this required about 2 hours. When the chlorine had been flushed out and the solvent and a small amount of phosphorus chlorides removed in vacuum, the substance obtained was treated at 0° with a mixture of ice and water until the acid reaction to congo disappeared. The weight of the substance, dried at 50-60°, was 12 g and the m.p. 115-120° (the fused substance was not quite clear). Recrystallization from ligroin (b.p.

•In a series of vat triazine dyes, a hypsochromic effect was observed from a hydroxyl in the ortho-position of a phenyl directly attached to the triazine ring [8].

90-110°) yielded 8.3 g (53.3%) of a substance with m.p. 118-119°. According to literature data, 2-phenyl-4,6-dichloro-1,3,5-triazine has m.p. 119-120° [11].

p- and o-Methoxyphenyldichlorotriazines were obtained analogously.

2-(4'-Methoxyphenyl)-4,6-dichloro-1,3,5-triazine formed colorless needles with m.p. 132-133°. Cl content in %: found 27.7; calculated 27.8.

2-(2'-Methoxyphenyl)-4,6-dichloro-1,3,5-triazine formed colorless needles with m.p. 139-140°. Cl content in %: found 27.5; calculated 27.8. According to literature data [8] the m.p. is 136°.

2-(2'-Hydroxyphenyl)-4,6-dichloro-1,3,5-triazine [7]. Dry hydrogen bromide (prepared in the usual way by the action of bromine on anthracene at room temperature and then purified by passage through a mixture of asbestos and anthracene followed by asbestos and phosphorus pentoxide) was passed for 8-10 hours at 150° into a solution of 3.2 g of o-methoxyphenyldichlorotriazine in 32 g of polychlorides (b.p. 160-180°) and then dry hydrogen chloride was passed for a period of 2 hours. Filtration to remove a small amount of impurities and removal of the polychlorides in vacuum yielded about 3 g of crude product. After recrystallization from a mixture of ligroin (b.p. 90-110°) and chlorobenzene, the substance melted at 153-154.5°; according to literature data, 2-(2'-hydroxyphenyl)-4,6-dichloro-1,3,5-triazine, recrystallized from methylcyclohexane, has m.p. 155° [7].

Dye (II). A solution of 1.13 g of phenyldichlorotriazine (m.p. 118-119°) in 20 ml of acetone was added at 40° with stirring to a solution of 5.02 g of 100% aminodisazo dye• and 150 ml of water and the reaction was carried at pH 6-6.5 with 1 N sodium carbonate solution added as required. The interaction lasted for 24 hours and 5 ml of sodium carbonate solution was used. Then (when the pH of the medium no longer changed) to the reaction mixture was added a solution of 1.4 g of 100% p-aminobenzeneazosalicylic acid•• in 35 ml of water, the mixture heated to boiling (80°) and the reaction carried out at this temperature with the pH kept at 6-6.5 by the gradual addition of 1 N sodium carbonate solution. The reaction lasted for 30 hours and the consumption of soda was 5 ml. Then 50 g of sodium chloride was added to the reaction mixture and the small amount of impurities removed by filtration. To hydrolyze the O-benzenesulfonic ester of the dye, 1 g of sodium hydroxide in 2.5 ml of water was added to the filtrate, the solution heated on a boiling water bath for 4 hours and the precipitated dye collected and purified by reprecipitation from aqueous solution. When developed on paper with water, the dye obtained gave a homogeneous chromatogram. The yield of 100% dye (in the purified preparation) was 4.3 g (65%).

Dyes (III) – (V) were obtained under analogous conditions. Data on the times of interaction of the aminoazo compounds with the aryldichlorotriazines are given in Table 2.

The light absorption of aqueous solutions of the dyes was determined on an SF-4 spectrophotometer.•••

SUMMARY

1. Green azo dyes based on 2-(4'- and 2'-methoxy- and 2'-hydroxyphenyl)-4,6-dichloro-1,3,5-triazines, which are not described in the literature, were synthesized; the dyes were characterized by the light-absorption spectrum in the visible region.

2. On the example of the dyes listed and their analogs based on 2-phenyl-4,6-dichloro-1,3,5-triazine and cyanuric chloride with the third chlorine atom in the latter replaced by an aniline residue it was shown that an imino group between the triazine and the phenyl had a small hypsochromic effect. Methoxy and hydroxy groups in the ortho- and para-positions of the phenyl directly attached to the triazine did not have a noticeable effect on the color, but suppressed the lability of the chlorine atoms in these triazine derivatives.

•We used the Na salt of the aminodisazo dye with the composition: O-benzoylsulfonic ester of H-acid → cresidine $\xrightarrow{\text{alkali}}$ H-acid. The dye was purified by three reprecipitations with sodium chloride from aqueous solution. It was established chromatographically that organic impurities were absent. The dye content of the substance was determined by reduction with vanadium sulfate.

••We used the Na salt of the dye which had been recrystallized from water; the dye was obtained by coupling diazotized aceto-p-phenylenediamine with salicylic acid and then hydrolysizing the acetyl group.

•••The determination was carried out by Z. E. Panfilova and I. A. Alatyrtseva.

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REACTION OF SULFUR CHLORIDE WITH 1,2,4-TRICHLOROBENZENE

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The action of sulfur chloride on aromatic halogen derivatives has been studied little. Information on the capacity of sulfur chloride to interact with these compounds is limited to two patents where the reactions with 1,2,3- and 1,2,4-trichlorobenzenes and 2,4-dichlorotoluene are described [1]. These reactions proceeded in the presence of anhydrous ferric chloride and led to the formation of disulfides, which could be reduced with zinc dust in an aqueous alcohol solution of sodium hydroxide to give the corresponding halogen-substituted thiophenols.

Wishing to study this reaction more closely, we investigated the action of sulfur chloride on 1,2,4-trichlorobenzene. The latter was chosen as the subject of the investigation since the expected product of subsequent reduction of the sulfurized trichlorobenzene (trichlorothiophenol) was of practical interest as a potential plasticizer of synthetic rubbers and an activator for the regeneration of rubber from vulcanizates.

An investigation of the behavior of sulfur chloride toward 1,2,4-trichlorobenzene showed that in the absence of catalytic agents, these substances did not react even on prolonged heating at the boiling point. However, in accordance with the data of the patents mentioned above, the same substances reacted vigorously in the presence of ferric chloride. We established that it was possible to use in this reaction metallic iron (evidently converted into ferric chloride under the reaction conditions) in the form of a powder, filings or the so-called iron sponge. The reaction was accompanied by evolution of hydrogen chloride, which became noticeable (in the presence of iron) at even 35-40°, proceeded very vigorously at 50-55° and was complete after 5-6 hours; raising the temperature to 70-80° caused considerable tar formation in the reaction product.

If 1,2,4-trichlorobenzene was treated with sulfur chloride alone (in the presence of iron), then the reaction product formed was a difficultly separable mixture of disulfide, trisulfide and monosulfide. A practically homogeneous product, namely hexachlorodiphenyl trisulfide (with a small amount of monosulfide), was obtained by treating 1,2,4-trichlorobenzene with sulfur chloride and elementary sulfur in amounts corresponding to the reaction equation.

$$2C_6H_3Cl_3 + S_2Cl_2 + S \xrightarrow{FeCl_3} (C_6H_2Cl_3)_2S_3 + 2HCl$$

Under these conditions, the yield of trisulfide was almost quantitative. As a result of side reactions, small amounts of 1,2,4,5-tetrachlorobenzene were formed together with the main product.

On the basis of the general rules of substituent orientation in the benzene nucleus, the trisulfide formed and also the di- and monosulfides we described below could be ascribed the structure of 2,4,5,2',4',5'-hexachloro derivatives. We propose to return to the problem of the direct proof of the structure we accepted for these compounds in another communication.

The method of sulfurizing 1,2,4-trichlorobenzene to 2,4,5,2',4',5'-hexachlorodiphenyl trisulfide was considerably simplified while the qualitative and quantitative results remained the same by preparing the sulfur chloride required for the reaction from sulfur and chlorine directly in the trichlorobenzene itself, when in accordance with the reaction equation presented above, sufficient chlorine to chlorinate 2/3 of all the sulfur was introduced into a suspension of sulfur in trichlorobenzene.

The formation of the sulfur chloride could also be combined with simultaneous sulfurization by introducing the calculated amount of chlorine into a solution or suspension of sulfur in trichlorobenzene with iron added. However this method of sulfurizing trichlorobenzene to hexachlorodiphenyl trisulfide was less convenient.

The preparation of 2,4,5,2',4',5'-hexachlorodiphenyl trisulfide by the action of sulfur chloride and elementary sulfur on 1,2,4-trichlorobenzene is an interesting example of the ready formation of trisulfides. On investigating the properties of this trisulfide, we observed that one sulfur atom in the molecule was readily eliminated. Thus, for example, nonprolonged boiling of the trisulfide in sodium sulfite solution formed 2,4,5,2',4',5'-hexachlorodiphenyl disulfide (m.p. 142-143°) with the simultaneous conversion of the sulfite to thiosulfate. Caustic alkalis like sodium hydroxide reacted similarly but in this case the alkali sulfide formed reduced the disulfide obtained to 2,4,5-trichlorothiophenol; this conversion may be expressed by the following equations:

$$3(C_6H_2Cl_3)_2S_3 + 6NaOH \longrightarrow 3(C_6H_2Cl_3)_2S_2 + Na_2SO_3 + 2Na_2S + 3H_2O,$$

$$(C_6H_2Cl_3)_2S_3 + Na_2SO_3 \longrightarrow (C_6H_2Cl_3)_2S_2 + Na_2S_2O_3,$$

$$\frac{4(C_6H_2Cl_3)_2S_2 + 6NaOH + 2Na_2S \longrightarrow 8C_6H_2Cl_3SNa + Na_2S_2O_3 + 3H_2O}{2(C_6H_2Cl_3)_2S_3 + 6NaOH \longrightarrow 4C_6H_2Cl_3SNa + Na_2S_2O_3 + 3H_2O}$$

The examination of conditions for sulfurizing 1,2,4-trichlorobenzene to 2,4,5,2',4',5'-hexachlorodiphenyl trisulfide and the behavior of the latter towards alkali sulfites and caustic alkalis led us to an extremely simple method for preparing 2,4,5-trichlorothiophenol consisting of treating the reaction mass formed by sulfurization of 1,2,4-trichlorobenzene with sodium hydroxide solution and simultaneously steam distilling the excess trichlorobenzene and then liberating the 2,4,5-trichlorothiophenol from the residual solution of trichlorothiophenolate with sulfur dioxide [2].

Completely pure and dry 2,4,5-trichlorothiophenol was quite a stable compound and was oxidized only slowly by the action of air to form the disulfide. This oxidation proceeded very noticeably in alkaline solution and more rapidly under the action of oxidants (iodine or sodium hypochlorite). The action of the latter on 2,4,5-trichlorothiophenol in the presence of excess diethylamine formed 2,4,5-trichlorobenzenesulfendiethylamide, an oily, liquid substance, which could be distilled in vacuum without decomposition. Trichlorobenzenesulfendiethylamide could be obtained from 2,4,5,2',4',5'-hexachlorodiphenyl disulfide by the same method.

In the presence of traces of organic solvents (for example alcohol) or moisture, 2,4,5-trichlorothiophenol reacted readily with finely divided sulfur. This reaction, which was accompanied by the evolution of hydrogen sulfide, proceeded even at normal temperature and led to the formation of 2,4,5,2',4',5'-hexachlorodiphenyl trisulfide.

EXPERIMENTAL

2,4,5,2',4',5'-Hexachlorodiphenyl Trisulfide (I). Into a suspension of 4.8 g of sulfur in 36.3 g of dry 1,2,4-trichlorobenzene (solid. pt. 15-16°, b.p. 212.5-214°), heated to 75-80°, was passed gaseous chlorine until the increase in weight was 3.5-3.6 g and then the reaction mass temperature was reduced to 50°, 0.1 g of powdered iron was added and the sulfurization carried out with continuous stirring at 50-55° until the evolution of hydrogen chloride ceased (after 5-6 hours). The excess trichlorobenzene (together with a small amount of 1,2,4,5-tetrachlorobenzene, m.p. 138-140°) was then steam distilled, the residual viscous mass extracted with 120-150 ml of benzene, the solution obtained (separated from water) decolorized by boiling with active charcoal and (I) isolated by dilution of the benzene solution with an equal volume of alcohol. The crude (I) was purified by recrystallization from a mixture of the same solvents. The yield of (I) was 22 g (96% calculated on the sulfur chloride).

Found %: Cl 46.09; S 20.85. $C_{12}H_4S_3Cl_6$. Calculated %: Cl 46.11; S 21.01.

The white, microscopic crystals of irregular form had m.p. 163-164°. They were soluble in benzene, chlorobenzene and chloroform and very slightly soluble in ethyl and methyl alcohols.

When a solution of (I) in benzene, chlorobenzene or trichlorobenzene was boiled with an aqueous solution of sodium sulfite, the trisulfide was converted into 2,4,5,2',4',5'-hexachlorodiphenyl disulfide (II); the action of sodium hydroxide under the same conditions led to the formation of 2,4,5-trichlorothiophenol (III).

2,4,5,2',4',5'-Hexachlorodiphenyl Disulfide (II). A solution of 2 g of (I) (m.p. 163-164°) in 25-30 ml of chlorobenzene was boiled and stirred for 1 hour with 50 ml of a 10% solution of crystalline sodium sulfite, the solvent removed by steam distillation and the residual solid product recrystallized from a mixture of benzene and alcohol. The yield of (II) was 1.8 g (96.5%). The conversion of (I) into (II) could be accomplished by the same method without the use of solvent, but in this case it required a somewhat longer time.

Found %: S 15.43. $C_{12}H_4S_2Cl_4$. Calculated %: S 15.29.

The almost colorless scales had m.p. 142-143° (from a mixture of chlorobenzene and alcohol). (II) was readily soluble in benzene, toluene and chlorobenzene, difficultly soluble in hot alcohol and insoluble in water. When treated with sodium sulfide and hydroxide, (II) was reduced to (III).

2,4,5-Trichlorothiophenol (III). a) From 1,2,4 -trichlorobenzene. Trichlorobenzene was sulfurized under the conditions given above in the description of the preparation of (I). The reaction mixture obtained was poured into a solution of 8-10 g of sodium hydroxide in 80 ml of water and the excess trichlorobenzene removed by steam distillation. During the distillation of the trichlorobenzene, (I) was reduced to (III), which dissolved in the form of trichlorothiophenolate. The solution of the latter was cooled to room temperature and filtered free from the insoluble precipitate of monosulfide, 100-120 ml of benzene added to the filtrate and (III) liberated by passing a stream of sulfur dioxide into the solution of trichlorothiophenolate with stirring. The (III) formed dissolved in benzene. Removal of the latter yielded 17-17.5 g (82%) of pure (III).

Found %: Cl 49.56; S 14.89. M 214.4. $C_6H_3SCl_3$. Calculated %: Cl 49.86; S 15.02. M 213.5.

The fine white needles had m.p. 112-113° (from aqueous alcohol) and b.p. 153-154° (17 mm) (in a nitrogen atmosphere). The product distilled in the form of long, lustrous needles, which were somewhat volatile in ordinary steam and distilled in superheated steam (170-180°). The substance was readily soluble in methyl and ethyl alcohols, aromatic hydrocarbons, chlorobenzene, trichlorobenzene and in aqueous solutions of alkali hydroxides and carbonates; it was very slightly soluble in water.

Action of Sulfur. A finely ground mixture of 2 g of trichlorothiophenol and 0.1 g of sulfur was moistened with several drops of alcohol in a beaker and left for several days at room temperature. The unchanged trichlorothiophenol was extracted by gently heating the mass with 10% sodium carbonate solution and the insoluble residue recrystallized from a mixture of benzene and alcohol. The substance obtained (m.p. 163-164°) was identical with (I) obtained by sulfurization of 1,2,4-trichlorobenzene (mixed melting point 163-164°).

b) From 2,4,5,2',4',5'-hexachlorodiphenyl disulfide (II). 18.9 g of (II) (m.p. 142-143°) was dissolved in a boiling solution of 5.5 g of $Na_2S \cdot 9H_2O$ and 2.8 g of NaOH in 100 ml of water. The cooled solution was filtered and (III) isolated from the filtrate by the method given in experiment "a". We obtained about 17 g (89.5%) of a substance with m.p. 112-113°, identical with (III) obtained by the action of sodium hydroxide on (II) (mixed melting point 112-113°).

2,4,5-Trichlorobenzenesulfendiethylamide (IV). a) From 2,4,5-trichlorothiophenol (III). A mixture of 125 ml of diethylamine and 70 ml of water was added at 45-50° to an aqueous suspension of 49 g of (III) (m.p. 112-113°) in 70-80 ml of water. With stirring, 105-110 ml of sodium hypochlorite solution (160-165 g of active chlorine per liter), which corresponded to approximately 17 g of active chlorine, was gradually added at 35-40° to the solution formed. During this operation a white flocculent precipitate was observed in the reaction liquid and this then changed into drops of an orange-yellow oil. The end of the reaction was determined by removing a 1-2 ml sample from the aqueous layer and acidifying it with dilute hydrochloric acid; when unreacted (III) was present in the solution, a precipitate formed (in this case a further small amount of hypochlorite was added to the reaction mixture). After the oxidation, 70-80 ml of water was added to the reaction mixture and the oily reaction product was separated, washed with water (2 × 100 ml) and dried in vacuum at 50-55° (10-15 mm). The dried product weighed 54-55 g. For purification it was vacuum distilled and a fraction with b.p. 143-147° (4 mm) collected; a second distillation yielded 44-44.5 g of pure (IV) (67-68%) with b.p. 146-146.5°, (4 mm).

Found %: C 42.38; H 4.29; Cl 37.17; S 11.15; N 4.85. $C_{10}H_{12}NSCl_3$. Calculated %: C 42.20; H 4.25; Cl 37.38; S 11.27; N 4.92.

The orange-yellow oil was stable under normal conditions and decomposed slowly only when boiled with dilute mineral acids. It was soluble in the usual organic solvents and insoluble in water.

b) From 2,4,5,2',4',5'-hexachlorodiphenyl disulfide (II). With stirring, a suspension of 42.5 g of (II) in 70-80 ml of water was treated at 45-50° with a mixture of 105 ml of diethylamine and 70 ml of water. The oxidation was then carried out under the conditions of the previous example by the addition of an amount of sodium hypochlorite corresponding to 8.5-8.6 g of active chlorine to the solution obtained. Purification of the product isolated by vacuum distillation yielded a substance with b.p. 146-146.5° (4 mm), which was identical with (IV) obtained from (III).

2,4,5,2',4',5'-Hexachlorodiphenyl Monosulfide (V). This substance was formed in very small amounts in the sulfurization of 1,2,4-trichlorobenzene with sulfur chloride in the experiments described above and isolated in the form of an insoluble precipitate in the reduction of (I) to (III). (V) was purified by precipitation with alcohol from a chlorobenzene solution. Purification yielded 0.6-0.7 g of (V) (about 3.5% calculated on the sulfur chloride).

Found %: C 36.70; H 0.96; Cl 54.04. $C_{12}H_4SCl_6$. Calculated %: C 36.60; H 1.02; Cl 54.20.

The white crystalline substance had m.p. 147-148°. It was soluble in benzene, toluene, chloroform and chlorobenzene, very slightly soluble in methyl and ethyl alcohols and insoluble in water.

SUMMARY

1. The conditions for reaction of 1,2,4-trichlorobenzene with sulfur chloride were investigated. It was established that these substances reacted at 35-55° in the presence of iron salts. In the presence of these catalysts, the reaction proceeded in practically one direction with the formation of 2,4,5,2',4',5'-hexachlorodiphenyl trisulfide by the combined action of sulfur chloride and elementary sulfur on 1,2,4-trichlorobenzene.

2. A simple method was developed for preparing 2,4,5-trichlorothiophenol, based on the reaction of 2,4,5,2',4',5'-hexachlorodiphenyl trisulfide with caustic alkalis.

3. Some of the properties of 2,4,5,2',4',5'-hexachlorodiphenyl tri-, di- and monosulfides and 2,4,5-trichlorothiophenol are described.

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CONVERSION OF BENZYL ALCOHOL ON GUMBRINE

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The catalytic dehydration of benzyl alcohol was investigated in a series of works published previously. The dehydrating agents used were sulfuric acid [1-5] and its salts [6, 7], boric anhydride [8], phosphoric acid [9], chlorides [9, 10] and Chasov Yar clay [11]. According to literature data the main products of the catalytic conversions of benzyl alcohol are dibenzyl ether and a tarry hydrocarbon with the composition $(C_7H_6)_x$.

In the present work an investigation was made of the conversion of benzyl alcohol over gumbrine activated with hydrochloric acid.

The effect of temperature and heating time on the yield of reaction products was studied (figure). With heating for one and a half hours, the alcohol was converted to a considerable extent even at 50° though the yield of ether-soluble reaction products was still insignificant. At 75° the conversion of benzyl alcohol increased sharply, exceeding 50%. The yield of ether-soluble products was then 27.1% (calculated on the original alcohol). When the heating temperature was raised to 100° the conversion of benzyl alcohol continued to increase while the amount of ether-soluble products hardly changed (28.5% calculated on the original alcohol). More than 90% of the benzyl alcohol was converted at 105° while the yield of ether-soluble products decreased somewhat. The noncorrespondence between the degree of conversion of the benzyl alcohol and the amount of ether-soluble products formed was connected with the formation of ether-insoluble tars which deposited on the catalyst.

Increasing the heating time from 1.5 to 3 hours (at 100°) led to almost complete conversion of the alcohol (the percent of unchanged alcohol was 1.3). The yield of ether-soluble products increased to 30.9% (calculated on the original alcohol).

The product obtained under the optimal conditions for the formation of ether-soluble materials (100° and a heating time of 3 hours) was investigated. The following substances were isolated: dibenzyl ether (main product), toluene, benzaldehyde, water, a substance with the composition $C_{21}H_{22}O$ and an ether-insoluble resin with the composition $(C_7H_6)_x$.

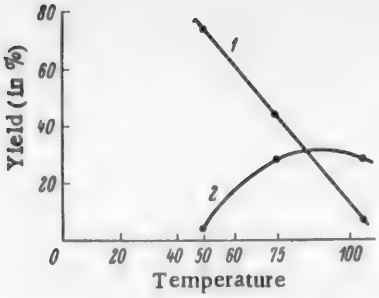
The formation of dibenzyl ether in the presence of an active clay with dehydrating properties was quite normal; it was accompanied by considerable evolution of water.

The formation of benzaldehyde and toluene could have proceeded in two directions.

1. Decomposition of dibenzyl ether by the scheme

$$C_6H_5CH_2OCH_2C_6H_5 \longrightarrow C_6H_5CH_3 + C_6H_5CHO$$

The possibility of this reaction was demonstrated in the work of Lachmann [12]. We carried out a special experiment on the decomposition of dibenzyl ether over gumbrine under the same conditions as in the main experiments with benzyl alcohol. Benzaldehyde and toluene were not detected among the decomposition products of the ether obtained. Consequently, the formation of benzaldehyde and toluene by this scheme is improbable under our conditions.



Dependence of degree of benzyl alcohol conversion and yield of ether-soluble products on temperature (heating time 1.5 hours). 1) Unchanged alcohol, 2) ether-soluble substance (without alcohol).

According to information available in the literature [13], benzaldehyde and toluene may be formed as a result of dehydrogenation of benzyl alcohol and subsequent hydrogenation of the benzaldehyde formed.

$$C_6H_5CH_2OH \xrightarrow{-H_2} C_6H_5CHO \xrightarrow{+2H_2} C_6H_5CH_3 + H_2O$$

In an experiment in which benzyl alcohol was heated with catalyst at 115-116°, we observed considerable evolution of gas, which caused the reaction mixture to swell, and the mass solidified due to the rapid formation of resin deposited on the catalyst. The gaseous products contained carbon monoxide and hydrogen (in the ratio 1:4.5). The presence of hydrogen in the gas makes this scheme very probable.

From the high-boiling products of benzyl alcohol conversion we also isolated a compound corresponding to the composition $C_{21}H_{20}O$. V. K. Teterin [11] isolated an analogous substance from the products of benzyl alcohol conversion on Chasov Yar clay and assigned it the structure of the ether from benzyl and benzylbenzyl alcohols.

We did not make a special investigation of this substance. Finally, the last product we isolated from the high-boiling residue was a resin with the composition $(C_7H_6)_x$, where x = 18-20. There are many reports in the literature on the formation of this substance in various catalytic conversions of benzyl alcohol.

EXPERIMENTAL

Benzyl alcohol was heated with hydrochloric-acid activated gumbrine on an oil bath in a round-bottomed flask fitted with a reflux condenser and a tube with a thermometer for controlling the temperature of the reaction mixture. In all experiments 20 g of benzyl alcohol and 12 g of catalyst were taken. After the heating, the liquid was decanted from the catalyst. The substance remaining on the catalyst was extracted with ether, added to the main mass after evaporation of the ether and distilled with a pear fractionating column. The degree of conversion of the benzyl alcohol was determined from the amount of the latter which distilled. To determine the optimal conditions for the formation of ether-soluble products we studied the effect of temperature (50, 75, 100 and 105°) and heating time (1.5 and 3 hours) on the degree of conversion of the original alcohol. The greatest yield of ether-soluble products was obtained with three hours heating at 100°. As a result of the investigation of the product obtained under these conditions (306 g), we isolated the following substances:

1) Unchanged benzyl alcohol (62.3 g) with b.p. 200-206°.

2) Toluene (6.3 g) with b.p. 110.5-111.5°, $n^{20}D$ 1.4961, d_4^{20} 0.8662.

Found: M 93.1, 95. $C_6H_5CH_3$. Calculated: M 92.

3) Benzaldehyde. This was isolated from a fraction with b.p. 118-182° (15.5 g) by shaking the fraction with sodium bisulfite. Heating the bisulfite compound with dilute hydrochloric acid liberated an oily substance with the characteristic odor of bitter almonds. On standing in air it changed into a crystalline substance with m.p. 121°, corresponding to the melting point of benzoic acid.

4) Dibenzyl ether (68.7 g).

B.p. 132.5-134.5° (6 mm), $n^{20}D$ 1.5617, d_4^{20} 1.0425.

Found %: C 84.71; H 7.31. M 197.3, 201. $C_{14}H_{14}O$. Calculated %: C 84.84; H 7.07. M 198.

5) A substance with the composition $C_{21}H_{20}O$ and b.p. 216-219° (5 mm); the product was oily and strongly fluorescent.

$n^{20}D$ 1.5940, d_4^{20} 1.0753. Literature data [11]: $n^{20}D$ 1.5940, d_4^{20} 1.0753.

Found %: C 87.51; H 7.18. M 265.8, 258.4. $C_{21}H_{20}O$. Calculated %: C 87.45; H 7.29. M 288.

6) A resin with the composition $(C_7H_6)_{18-20}$ (16.3 g); b.p. above 234° (5 mm); the substance was a clear, yellow-brown solid. The substance was readily soluble in toluene and precipitated from this solvent by ether to give a sticky, viscid resin. The resin was purified by several reprecipitations and then the product was pressed on a porous plate.

Found %: C 93.25; H 6.52. M 1779, 1652. $(C_7H_6)_{18-20}$. Calculated %: C 93.33; H 6.56.

SUMMARY

1. The conversion of benzyl alcohol on activated gumbrine clay under mild conditions was studied.

2. The reaction products yielded dibenzyl ether, toluene, benzaldehyde, a substance with the composition $C_{21}H_{20}O$ and a resin with the composition $(C_7H_6)_X$.

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INVESTIGATIONS IN THE FIELD OF CONJUGATED SYSTEMS

CI. OXIDATION OF VINYLALKYLACETYLENES WITH BENZOYL HYDROPEROXIDE*

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In a series of works by N. M. Malenok and other authors [1, 2] it was shown that in the oxidation of vinylacetylene hydrocarbons by hydroperoxides, oxygen added to the ethylene bond in the first instance with the exclusive formation of acetylene monoxides. Ozone also added similarly to vinylacetylenes [2].

In this work quite complicated vinylacetylene or diene hydrocarbons were oxidized. The oxidation of the simplest vinylalkylacetylenes was not investigated.

Continuing a systematic study of the reactions of vinylalkylacetylenes, we undertook experiments on the oxidation of two hydrocarbons, namely vinylethyl- and vinylbutylacetylenes, by benzoyl hydroperoxide. These experiments were also of interest, as in attempts to obtain pure oxides of higher vinylalkylacetylenes through the bromohydrins, we encountered serious difficulties: the low solubility of the bromohydrins in water made it impossible to free them from dibromides by extraction with water.

The oxidation of the two hydrocarbons yielded acetylene oxides. In its constants, vinylethylacetylene oxide was found to be identical with the oxide of the same hydrocarbon obtained previously through the bromohydrin [3].

For a more complete identification, the infrared spectra of the two samples of vinylethylacetylene oxide were plotted. Analysis of the data obtained showed first of all that in both cases we were dealing with acetylene compounds. They did not absorb in the region of 1600-1680 cm^{-1}, which is characteristic of double bond frequencies. The frequency of the acetylene bond (2250 cm^{-1}) was extremely intense, which may be explained by its conjugation with the oxide bond. The frequency 1250 cm^{-1} and possibly others, for example 1137 and 1160 cm^{-1}, were apparently connected with the presence of the oxide grouping [4]. It is also interesting to note that the spectra of both oxide samples had valence frequencies of C–H bonds, which usually appear in the spectra of substances with the $CH_2=C$ grouping (3064 cm^{-1}). This is yet another fact indicating the similarity of the oxide grouping to a double bond [5].

The spectrum of the oxide sample obtained by oxidation of the hydrocarbon differed from the spectrum of the same oxide obtained through the bromohydrin only in the presence of a band of average intensity at about 1728 cm^{-1}. This frequency also occurs in the spectra of diene oxides obtained by the same method [2].

Acetylene compounds frequently absorb at 1700 cm^{-1} [6]; however, the absence of a band in this region for the oxide obtained through the bromohydrin excludes the possibility of assigning it to vibrations of the acetylene grouping. It evidently belonged to impurities.

The frequency 1728 cm^{-1} could be ascribed to a compound with the grouping $-C\overset{\diagdown\,\diagup}{=}C-$ (O), which could be obtained by oxidation of vinylethylacetylene. Spectra of compounds of this type have not been described. How-

*Enyne compounds. XXVII.

ever, the absence of valence and deformation frequencies of the vinyl group from the spectra of both oxide samples excludes this hypothesis.

It is most likely that the appearance of the frequency 1728 cm^{-1} was due to the fact that the oxide sample obtained by oxidation of the hydrocarbon may have contained traces of a carbonyl compound with an unconjugated carbonyl group, formed due to partial isomerization of the oxide during its formation.

The spectrum of vinylbutylacetylene oxide was similar to the spectrum of vinylethylacetylene. Here, the frequency of the acetylene bond also had a high intensity. There was also the carbonyl group frequency (1728 cm^{-1}). In addition, the spectrum of this oxide also contained the frequencies 1669, 982 and 927 cm^{-1} at a low intensity and these may be ascribed to oscillations of the diene grouping. However, it is most probable that the frequency 1669 cm^{-1} pertained to traces of ketone with a conjugated carbonyl group or was an overtone while the frequencies 982 and 927 cm^{-1} may refer to C—C oscillations.

Thus, in the case of vinylethylacetylene, it may be stated that the addition of oxygen in the oxidation of this hydrocarbon by benzoyl hydroperoxide occurs in the first instance at the ethylene bond only, while in the case of vinylbutylacetylene it can only be said that this orientation prevails.

EXPERIMENTAL

Benzoyl hydroperoxide was prepared by the usual method [7]. The oxidation was carried out at 0-5° in chloroform solution. The course of the reaction was followed by iodometric titration of samples from the reaction mixture. In the oxidation of vinylethylacetylene, the reaction was 70% complete in one day, 84% in two days and 98% in 5 days. In the case of vinylbutylacetylene, 92% of the hydroperoxide had reacted after one day and the reaction was complete after two days (99.5% of the hydroperoxide had reacted). The yield of oxides was 40-45% on the hydrocarbon reacted. In both cases part of the hydrocarbon did not react and we observed the formation of considerable amounts of high-boiling tarry products, which were not examined more closely.

Vinylethylacetylene Oxide (1,2,-epoxyhexyne-3).

B.p. 66-67° (50 mm), 140-141° (758 mm), d_4^{20} 0.9181, $n^{20}D$ 1.4520, MR_D 28.25; calc. 27.35.

Found %: C 74.98, 75.20; H 8.70, 8.85. C_6H_8O. Calculated %: C 74.97; H 8.38.

IR-Spectrum:* 787 s, 855 v.s., 938 s, 994 av., 1025 w, 1060 w, 1137 s, 1166 s, 1250 s, 1319 s, 1378 v.s., 1435 av., 1461 s, 1565 w, 1728 av., 2249 s, 2854 av., 2885 s, 2919 s, 2944 s, 2981 v.s., 3063 av. cm^{-1}

The same oxide obtained from the bromohydrin had the constants [3]: b.p. 140-141°, d_4^{20} 0.9182, $n^{20}D$ 1.4530.

The infrared spectrum differed from that given above only in the absence of the frequency 1728 cm^{-1}.

Vinylbutylacetylene Oxide (1,2-epoxyoctyne-3).

B.p. 80-80.5° (20 mm), d_4^{20} 0.8960, $n^{20}D$ 1.4550, MR_D 37.60; calc. 36.59.

Found %: C 77.27, 77.94; H 9.89, 10.12. $C_8H_{12}O$. Calculated %: C 77.38; H 9.74.

IR-Spectrum: 727 av., 749 av., 790 s, 848 s, 870 s, 885 s, 927 av., 961 s, 973 av., 982 s, 995 av., 1028 w, 1047 w, 1054 w, 1069 w, 1105 av., 1136 s, 1164 s, 1250 s, 1301 av., 1329 av., 1378 v.s., 1433 s, 1464 v.s., 1572 w, 1669 av., 1728 av., 2204 w, 2248 s, 2738 w, 2868 s, 2676 s, 2938 v.s., 2964 v.s., 3064 av cm^{-1}.

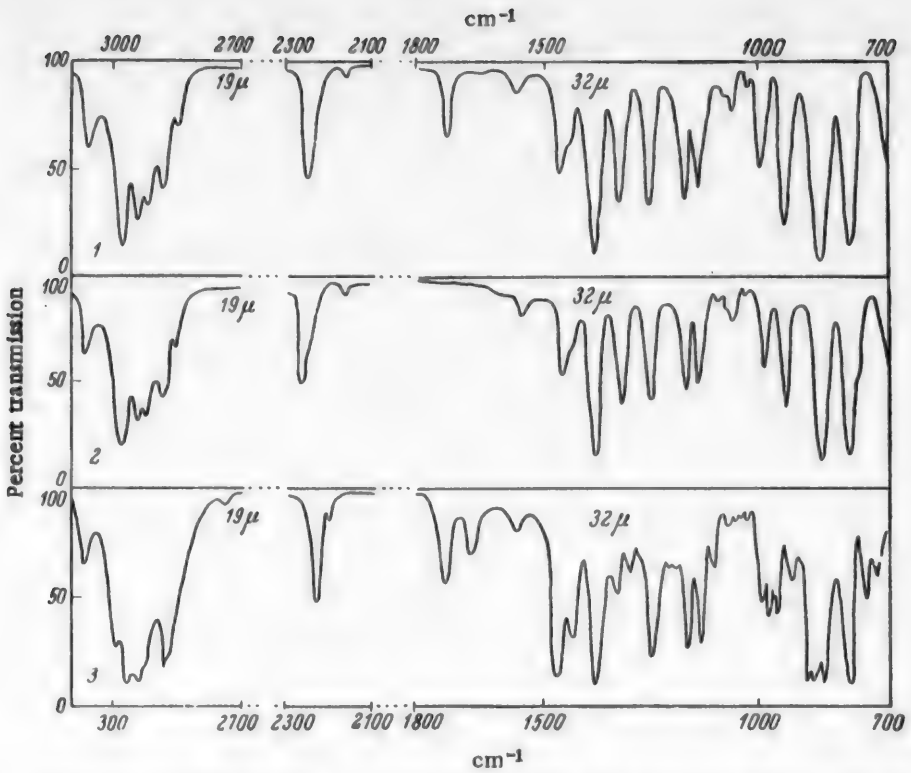
SUMMARY

1. The order of the oxidation of vinylalkylacetylenes by benzoyl hydroperoxide was investigated on the example of vinylethyl- and vinylbutylacetylenes.

2. It was shown that the formation of the first oxide ring occurred exclusively or almost exclusively at the double bond.

3. Vinylbutylacetylene oxide is described for the first time.

*The infrared spectra were plotted on an IKS-14 apparatus with an NaCl prism in the region up to 1900 cm^{-1} and then with an LiF prism. The layer thickness was 0.032 mm.



Infrared transmission spectra. 1) Vinylethylacetylene oxide obtained by oxidation of hydrocarbon; 2) the same oxide obtained through the bromohydrin; 3) vinylbutylacetylene oxide.

4. Certain phenomena in the infrared spectra of the acetylene oxides were analyzed.

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INVESTIGATIONS IN THE FIELD OF CONJUGATED SYSTEMS

CII. DIRECTION OF HYDRATION OF VINYLALKYLACETYLENES•

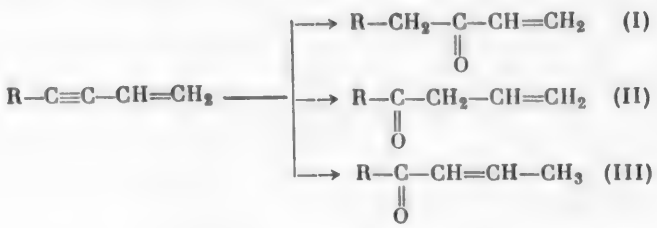
B. S. Kupin and A. A. Petrov

Lensoviet Technological Institute Leningrad

The hydration of acetylene and its derivatives has been the subject of many investigations with the use of homogeneous and heterogeneous catalysts [1-3]. The hydration of vinylacetylene hydrocarbons has mainly been studied on the example of vinylacetylene and its homologs with a terminal acetylene grouping, when in all cases the oxygen was added to the second carbon of the acetylene grouping: vinylacetylene gave methyl vinyl ketone [4, 5], isopropenylacetylene gave methyl isopropenyl ketone [6, 7] and β-tert-butylvinylacetylene gave 4,4-dimethyl-3-methenepentanone-2 [8].

In recent years, considerable attention has also been given to the hydration of divinylacetylene compounds leading to the formation of various dienones, from which physiologically active compounds could be obtained [9]. A peculiarity of the hydration of divinylacetylenes is the formation of ketones with a carbonyl group at the most substituted unsaturated radical [9, 10].

We carried out experiments on the hydration of four vinylalkylacetylenes (vinylmethyl-, vinylethyl-, vinylpropyl- and vinylbutylacetylenes) in the presence of mercuric sulfate. In each case one might have expected the formation of three isomeric ketones differing sharply in constants.



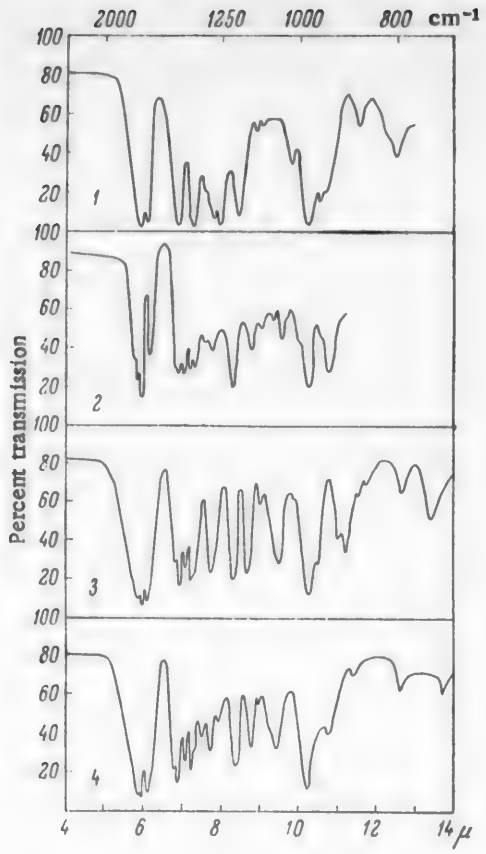
In actual fact we obtained predominantly alkyl propenyl ketones (III) with some alkyl allyl ketones (II). The structure of the ketones was demonstrated by comparison of their constants and infrared spectra with literature data and also by studying the saturated ketones formed when they were hydrogenated.

The constants and infrared spectra of the methyl propenyl, ethyl propenyl and propyl propenyl ketones we obtained were extremely close to those reported for these compounds in the literature [11, 12]. All the spectra contained an intense frequency in the region of 970 cm^{-1} (the $-CH=CH-$ grouping); compounds with a vinyl grouping were only present in small amounts (a weak band at 6110 cm^{-1} was found).

Hydrogenation of all the hydration products over $Pd/CaCO_3$ gave predominantly alkyl propyl ketones, which are described in the literature [12].

The hydration of vinylalkylacetylenes apparently proceeds by a 1,2-addition scheme at the acetylene bond with the formation of alkyl allyl ketones, which isomerize in an acid medium to alkyl propenyl ketones [13]. We consider the addition of water in the 1,4-position, which leads to the same result, improbable.

•Enyne compounds. XXVIII.

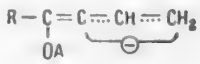


Infrared transmission spectra of hydration products. 1) Vinylmethylacetylene, 2) vinylethylacetylene, 3) vinylpropylacetylene, 4) vinylbutylacetylene.

It should be noted that the rate of water addition decreased with an increase in the hydrocarbon radical. This forced us to use heating in carrying out the reaction with vinylpropylacetylene.

Comparison of the data of this article with the previously described results of experiments on the addition of water to vinylalkylacetylenes over heterogeneous catalysts• [3] and the addition of alcohols in the presence of potassium hydroxide [14] indicates that the order of addition of these nucleophilic addends does not depend on the nature of the catalyst, medium or reagent and is determined by the structure of the hydrocarbon.

The order of addition of water and alcohols does not correspond to the order of addition of hydrogen halides and in our opinion this is connected with differences in the mechanism of these reactions. The addition of water only occurs at the acetylene bond and has a nucleophilic character and in this case the most stable intermediate ion would be the anion:



The reaction with hydrogen halides begins with electrophilic attack on the acetylene bond also and proceeds through a π-complex and then through a cation that is most stable in this case:



EXPERIMENTAL

Hydration of Vinylmethylacetylene. 17 g of hydrocarbon was stirred vigorously with a solution of 6 g of HgO in 350 ml of 11% sulfuric acid for 6 hours. The liquid was then steam distilled. The upper layer, consisting of ketone and unreacted hydrocarbon was separated. The ketone was salted out from the lower layer with ammonium sulfate. We obtained 7.8 g (52% on the hydrocarbon reacted) of methyl propenyl ketone with b.p. 120-122°, d_4^{20} 0.8583, $n^{20}D$ 1.4360.

Found %: C 71.18, 71.24; H 9.59, 9.84. C_5H_8O. Calculated %: C 71.42; H 9.53.

IR-Spectrum: 798 (av), 864 (av), 949 (s.), 976 (v.s.), 1021 (av), 1104 (w), 1120 (w), 1183 (v.s.), 1257 (v.s.), 1279 (s.), 1314 (av) ; 1293 (s.), 1372 (v.s.), 1444 (v.s.), 1638 (v.s.), 1687 (v.s.), cm^{-1} (figure, curve 1).

2,4-Dinitrophenylhydrazone: m.p. 153° (from alcohol).

All these data are close to those presented in the literature for the trans-form of methyl propenyl ketone [15].

When 5.6 g of ketone in 20 ml of methyl alcohol was reduced in the presence of 8 g of $Pd/CaCO_3$, 1571 ml (97.5%) of H_2 (772 mm, 18°) was absorbed. The reaction mixture was decanted from the catalyst, diluted with ether and washed with a saturated solution of calcium chloride. Removal of the ether yielded 3.7 g of methyl propyl ketone with b.p. 101-102°, d_4^{20} 0.8091, $n^{20}D$ 1.3960.••

•The work was carried out simultaneously with ours with a sample of vinylethylacetylene we provided, as was stated in publication [3].

••The IR-spectrum of the substance practically coincides with that of a mixture of 85% methyl propyl (A) and 15% of diethyl ketone (B). Characteristic frequencies: (A) 1168 and (B) 1124 cm^{-1}.

The 2,4-dinitrophenylhydrazone had m.p. 141°, which corresponds with literature data [12].

Hydration of Vinylethylacetylene. Under the conditions described above, 30 g of hydrocarbon yielded 8 g (38%) of ethyl propenyl ketone with b.p. 135-137°, d_4^{20} 0.8492, $n^{20}D$ 1.4350.

Found %: C 73.62, 73.71; H 10.30, 10.45. $C_6H_{10}O$. Calculated %: C 73.47; H 10.20.

IR-Spectrum: 929 (s.), 940 (w.) 974 (s.), 995 (v.w.), 1043 (av.), 1105 (av.), 1136 (av.), 1202 (s.), 1289 (w.), 1322 (w.), 1362 (s.), 1380 (s.), 1421 (s.), 1450 (s.), 1464 (s.), 1638 (s.), 1680 (v.s.), 1708 (w.) cm^{-1} (figure, curve 2).

When 3 g of ketone in 15 ml of methanol was hydrogenated in the presence of 6 g of $Pd/CaCO_3$, 690 ml (94%) of H_2 (771 mm, 18°) was absorbed. We obtained 1.5 g of ethyl propyl ketone with b.p. 122-124°, d_4^{20} 0.8187, $n^{20}D$ 1.3997.

The 2,4-dinitrophenylhydrazone had m.p. 130°, which corresponds with literature data [12].

Hydration of Vinylpropylacetylene. Into a two-necked flask with a reflux condenser were placed 32 g of hydrocarbon and a solution of 10 g of HgO in 600 ml of 15% sulfuric acid and the mixture stirred vigorously at 70-80° for 6 hours. The mixture was then treated as in the previous experiments. We obtained 12 g (43%) of propyl propenyl ketone with b.p. 155-157°, d_4^{20} 0.8527, $n^{20}D$ 1.4393.

Found %: C 74.93, 75.28; H 10.78, 10.53. $C_7H_{12}O$. Calculated %: C 75.00; H 10.71.

IR-Spectrum: 734 (av.), 790 (w.), 853 (w.), 867 (w.), 892 (av.), 906 (w.), 954 (av.), 972 (v.s.), 1012 (v.s.), 1050 (s.), 1112 (v.w.), 1154 (s.), 1197 (s.), 1289 (s.), 1298 (w.), 1312 (w.), 1348 (v.w.), 1367 (av.), 1380 (s.), 1410 (av.), 1446 (s.), 1460 (w.), 1633 (s.), 1675 (v.s.), 1692 (av.), cm^{-1} (figure, curve 3).

8.5 g of ketone in 25 ml of methyl alcohol was reduced in the presence of 10 g of $Pd/CaCO_3$. 1767 ml (91%) of H_2 (756 mm, 19°) was absorbed. Distillation yielded 5.5 g of dipropyl ketone with b.p. 142.5-143.5°, d_4^{20} 0.8267, $n^{20}D$ 1.4078, which corresponds to literature data [12].

2,4-Dinitrophenylhydrazone: m.p. 73-74° [12].

Hydration of Vinylbutylacetylene. Heating 36 g of hydrocarbon in 700 ml of 15% sulfuric acid with 11 g of HgO yielded 9 g (40%) of butyl propenyl ketone with b.p. 176-178°, d_4^{20} 0.8515, $n^{20}D$ 1.4405.

Found %: C 76.43, 76.12; H 11.33, 11.31. $C_8H_{14}O$. Calculated %: C 76.19; H 11.11.

IR-Spectrum: 729 (w.), 790 (w.), 877 (w.), 930 (av.), 973 (v.s.), 1059 (s.), 1114 (v.w.), 1137 (w.), 1191 (s.), 1253 (w.), 1287 (av.), 1326 (av.), 1368 (av.), 1380 (s.), 1411 (av.), 1446 (s.), 1464 (av.), 1633 (s.), 1677 (v.s.), 1692 (v.s.), cm^{-1} (figure, curve 4).

Reduction of 6 g of unsaturated ketone yielded 4 g of propyl butyl ketone with b.p. 164-166°, d_4^{20} 0.8159, $n^{20}D$ 1.4145. The semicarbazone had m.p. 99-100°.

Literature data: b.p. 165-168°. Semicarbazone: m.p. 100-101° [16].

SUMMARY

1. The hydration of vinylmethyl-, vinylethyl-, vinylpropyl- and vinylbutylacetylenes in the presence of mercuric sulfate was studied.

2. It was shown that alkyl propenyl ketones were formed predominantly in all cases.

3. The reverse order of addition of water in comparison with that of hydrogen halides was explained by the nucleophilic character of the reaction and the ease of redistribution of the electron density in vinylalkylacetylene molecules due to the effect of the alkyl groups on the enyne system.

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SYNTHETIC ANESTHETICS:

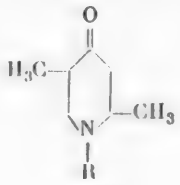
γ-PIPERIDONES, γ-PIPERIDOLS, AND THEIR ESTERS

I. N. Nazarov, N. S. Prostakov, N. N. Mikheeva

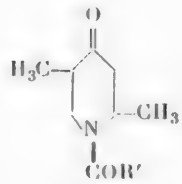
and S. L. Davydova

Moscow Institute of Fine Chemical Technology

Continuing work on the synthesis of γ-piperidols and their esters – analogs of promedol and isopromedol [1], we prepared a series of new γ-piperidones through the alkylation or acylation of 2,5-dimethyl-4-piperidone [2, 3].



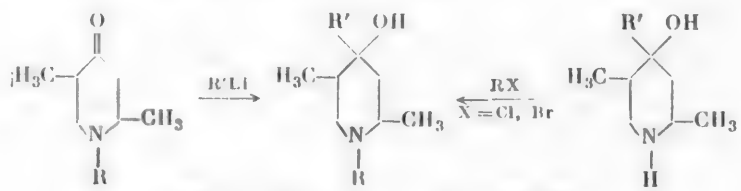
(I) R = $CH_2CH_2C_6H_5$; (II) R = $CH_2CH{=}CHC_6H_5$;
(III) R = $CH_2CH_2C_6H_4NO_2$-; (IV) R = $C_6H_5CHCOOCH_3$.



(V) R′ = $H_2NC_6H_4$-n; (VI) R′ = 3,4,5-$(CH_3O)_3C_6H_2$;
(VII) R′ = β-C_5H_4N; (VIII) R′ = α-C_4H_3O;
(IX) R′ = $CH_2CH_2N(C_2H_5)_2$; (X) R′ = $OCH_2C_6H_5$.

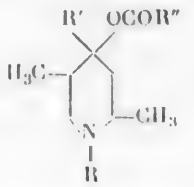
We prepared 1-β-phenylethyl- (I), 1-γ-phenylallyl- (II), 1-β-p-nitrophenylethyl- (III), 1-phenylcarbomethoxymethyl- (IV), 1-(3′,4′,5′-trimethoxybenzoyl)- (VI), 1-nicotinoyl- (VII), 1-furoyl- (VIII), 1-β-diethylaminopropionyl- (IX), and 1-carbobenzoxy- (X) 2,5-dimethyl-4-piperidones. 1-p-Aminobenzoyl-2,5-dimethyl-4-piperidone (V) was obtained by reduction of the nitro group of 1-p-nitrobenzoyl-2,5-dimethyl-4-piperidone, which was described by us earlier [3]. On hydrogenolysis of piperidone (X) the original 2,5-dimethyl-4-piperidone was formed.

The synthesis of γ-piperidols was carried out either through the reaction of the corresponding piperidones with organolithium compounds or through replacement of the hydrogen of the secondary amino group of 2,5-dimethyl-4-phenyl-4-piperidol [4] by the corresponding radicals.



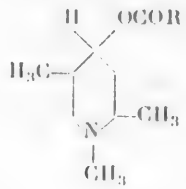
(XI) R = CH_3, R′ = o-$CH_3C_6H_4$;
(XII) R = CH_3, R′ = α-C_4H_3N;
(XIII) R = $CH_2CH_2C_6H_5$, R′ = C_6H_5;
(XIV) R = $CH_2CH{=}CHC_6H_5$, R′ = C_6H_5;
(XV) R = COC_5H_4N-α, R′ = C_6H_5.

1-Methyl-4-o-tolyl(XI),1-methyl-4-α-pyridyl- (XII), 1-β-phenylethyl-4-phenyl- (XIII), 1-γ-phenylallyl-4-phenyl- (XIV), and 1-nicotinoyl-4-phenyl- (XV) 2,5-dimethyl-4-piperidols were prepared. On esterification of the piperidols by means of acid chlorides the following esters were obtained: 1-methyl-4-o-tolyl- (XVI), 1-β-phenylethyl-4-phenyl- (XVIII), 1-γ-phenylallyl-4-phenyl- (XIX), and 1-methyl-4-α-pyridyl- (XX) 2,5-dimethyl-4-piperidyl propionates, the trimethoxybenzoate (XVII) of the α-, β-, and γ-isomers of 1,2,5-trimethyl-4-phenyl-4-piperidol (I), 1-diethylaminoacetyl-2,5-dimethyl-4-phenyl-4-piperidyl propionate (XXI), and 1-β-phenylethyl-2,5-dimethyl-4-phenyl-4-piperidyl phenoxyacetate (XXII).



(XVI) R = CH_3, R′ = o-$CH_3C_6H_4$, R″ = C_2H_5
(XVII) R = CH_3, R′ = C_6H_5, R″ = 3,4,5-$(CH_3O)_3C_6H_2$
(XVIII) R = $CH_3CH_2C_6H_5$, R′ = C_6H_5, R″ = C_2H_5
(XIX) R = $CH_2CH{=}CHC_6H_5$, R′ = C_6H_5, R″ = C_2H_5
(XX) R = CH_3, R′ = α-C_5H_4N, R″ = C_2H_5
(XXI) R = $COCH_2N(C_2H_5)_2$, R′ = C_6H_5, R″ = C_2H_5
(XXII) R = $CH_2CH_2C_6H_5$, R′ = C_6H_5, R″ = $CH_2OC_6H_5$.

For pharmacological testing, the following 1,2,5-trimethyl-4-piperidol esters were prepared in the same way: the β-phenylmercaptopropionate (XXIII), diethylaminoacetate (XXIV), and N-piperidylacetate (XXV). The results of pharmacological tests of the compounds obtained will be published separately.



(XXIII) R = $CH_2CH_2SC_6H_5$; (XXIV) R = $CH_2N(C_2H_5)_2$;
(XXV) R = $CH_2NC_5H_{10}$.

EXPERIMENTAL

1-β-Phenylethyl-2,5-dimethyl-4-piperidone (I). Twenty-five g of 2,5-dimethyl-4-piperidone, 36 g of β-phenylethyl bromide, 38 g of calcined potash, and 20 ml of acetone were heated and stirred in a water bath for 15 hours. After the acetone was distilled off, the residue was neutralized with 15% hydrochloric acid (to congo). The water layer was saturated with sodium hydroxide and treated with ether. From the ethereal extract, after drying, there was obtained 18.3 g of piperidone (I), m.p. 72-74° (from benzine).

Found %: N 6.16, 6.38. $C_{15}H_{21}ON$. Calculated %: N 6.06.

1-γ-Phenylallyl-2,5-dimethyl-4-piperidone (II). Fourteen g of 2,5-dimethyl-4-piperidone, 21 g of γ-phenylallyl bromide, 22.8 g of potash, and 10 ml of acetone were brought into reaction. The reaction was carried out similarly. On distillation of the residue from the ethereal extract of the basic reaction products, there were obtained 2 g of the original piperidone and 13.1 g of piperidone (II), b.p. 175° (2.5 mm).

Found %: N 5.49, 5.59. $C_{16}H_{21}ON$ Calculated %: N 5.76.

1-β-Nitrophenylethyl-2,5-dimethyl-4-piperidone (III). An 8.7 g quantity of 2,5-dimethyl-4-piperidone, 7 g of β-p-nitrophenylethyl bromide, 14 g of potash, and 8 ml of acetone were heated in a water bath for 20 hours. After the basic reaction products were separated out in the usual manner, an oily residue was obtained, from which 1.8 g of piperidone (III), m.p. 84-87°, was isolated after recrystallization from acetone.

Found %: N 10.72, 10.70. $C_{15}H_{20}O_3N_2$. Calculated %: N 10.14.

1-Phenylcarbomethoxymethyl-2,5-dimethyl-4-piperidone (IV). To 8 g of 2,5-dimethyl-4-piperidone and 13 g of methyl bromophenylacetate (b.p. 138-140° at 3 mm) was added a slurry of 16 g of potash and acetone. The mixture was heated and stirred for 15 hours. The reaction products were then extracted with ether and distilled in vacuo. There was obtained 9 g of piperidone (IV), b.p. 162-164° (5 mm), m.p. 86-89° (from benzine).

Found %: N 5.23, 4.89. $C_{16}H_{21}O_3N$. Calculated %: N 5.09.

1-p-Aminobenzoyl-2,5-dimethyl-4-piperidone (V). To a solution of 16 g of 1-p-nitrobenzoyl-2,5-dimethyl-4-piperidone (m.p. 138-140°) in 70 ml of ethanol, heated to 50°, was added a solution of 40 g of stannous chloride in 50 ml of alcohol and 50 ml of concentrated hydrochloric acid. After heating in a water bath for 6 hours the alcohol was distilled off and the residue treated with soda and extracted with benzene. After drying followed by distillation of part of the benzene there was obtained 13.5 g of piperidone (V), m.p. 137-140°.

Found %: N 11.28, 11.16. $C_{14}H_{18}O_2N_2$. Calculated %: N 11.38.

Hydrochloride of (V) – m.p. 172° (decomp.).

Found %: N 10.22, 10.35. $C_{14}H_{19}O_2N_2Cl$. Calculated %: N 9.91.

1-(3',4',5'-Trimethoxybenzoyl)-2,5-dimethyl-4-piperidone (VI). To 8 g of 2,5-dimethyl-4-piperidone, a solution of 6 g of trimethoxybenzoyl chloride (m.p. 80-81°) in 30 ml of benzene was added with stirring and ice-water cooling. Stirring and cooling were continued for 2 hours. The separated 2,5-dimethyl-4-piperidone hydrochloride (4.6 g) was filtered out and the reaction products fractionated in vacuo. There were obtained 1.3 g of the original piperidone and 6.5 g of piperidone (VI), b.p. 220-222° (2.5 mm); m.p. 103-104° (from ether).

Found %: N 4.34, 4.31. $C_{17}H_{23}O_5N$. Calculated %: N 4.36.

1-Nicotinoyl-2,5-dimethyl-4-piperidone (VII). A 41.5 g quantity of 2,5-dimethyl-4-piperidone, 23 g of nicotinoyl chloride (b.p. 92-100° at 12 mm), and 130 ml of benzene were refluxed for 5 hours. After the benzene was distilled off, 2.5 g of the original piperidone and 12 g of an immobile liquid with b.p. 202-205° (2 mm) were obtained. From the latter there was isolated 0.7 g of crystals with m.p. 66-67° (from ether), corresponding to one of the stereoisomeric forms of (VII).

Found %: C 67.31, 67.52; H 6.99, 7.05. $C_{13}H_{16}O_2N_2$. Calculated %: C 67.24; H 6.90.

Hydrochloride – m.p. 154-156° (from alcohol).

Found %: N 9.92, 9.99. $C_{13}H_{17}O_2N_2Cl$. Calculated %: N 9.77.

Oxime – m.p. 141-144° (from alcohol).

Found %: N 15.88, 15.97. $C_{13}H_{17}O_2N_3 \cdot H_2O$. Calculated %: N 15.85.

After the crystals with m.p. 66-67° were separated out, there remained a mixture of stereoisomeric piperidones (VII); from the latter there was obtained an oxime with m.p. 169-170° (from alcohol), obviously corresponding to the other stereoisomeric form of (VII).

Found %: N 16.20, 16.28. $C_{13}H_{17}O_2N_3 \cdot H_2O$. Calculated %: N 15.85.

1-Furoyl-2,5-dimethyl-4-piperidone (VIII). Twenty g of 2,5-dimethyl-4-piperidone, 10 g of furoyl chloride, and 150 ml of benzene were refluxed for 3 hours. After the benzene was distilled off, the residue was heated with 20 ml of acetone. The crystals of the hydrochloride of the original piperidone, which separated on cooling, were filtered out and the residue distilled in vacuo. There was obtained 13.4 g of piperidone (VIII), b.p. 167-168° (3 mm).

Found %: N 6.25, 6.22. $C_{12}H_{15}O_3N$. Calculated %: N 6.33.

Oxime – m.p. 168-171°.

Found %: N 11.92, 11.58. $C_{12}H_{16}O_3N_2$. Calculated %: N 11.86.

1-β-Diethylaminopropionyl-2,5-dimethyl-4-piperidone (IX). To a solution of 16.5 g of β-chloropropionyl chloride in 100 ml of benzene, cooled with ice water, was added 33 g of 2,5-dimethyl-4-piperidone. The mixture was then refluxed for 5 hours. The separated hydrochloride (20 g) of the original piperidone was filtered out and the benzene distilled off. Thirty g of an immobile oil remained; 15 g of this product, 12.5 g of diethylamine, and 100 ml of benzene were heated in a water bath for 5 hours. The diethylamine hydrochloride (4.6 g) was filtered out and the remainder distilled in vacuo. There was obtained 12.2 g of a substance with b.p. 133-136° (2 mm), $n^{20}D$ 1.4997. This in turn gave the picrate of piperidone (IX). M.p. 124° (from alcohol).

Found %: N 14.72, 14.79. $C_{20}H_{29}O_9N_5$. Calculated %: N 14.49.

Hydrochloride of piperidone (IX) was an uncrystallizable oil.

1-Carbobenzoxy-2,5-dimethyl-4-piperidone in 50 ml of toluene was added 150 g of a 23% solution of benzyl chloroformate in toluene. The mixture was gently refluxed for 4 hours. The toluene solution was decanted from the separated 2,5-dimethyl-4-piperidone hydrochloride. The toluene was driven off and the residue distilled in vacuo. There was obtained 41 g of piperidone (X). B.p. 185-186° (2 mm), $n^{20}D$ 1.5313.

Found %: N 5.32, 5.59. $C_{15}H_{19}O_3N$. Calculated %: N 5.36.

A 3.5 liter volume of hydrogen was passed into a solution of 8.8 g of (X) in 100 ml of anhydrous methanol in the presence of 5 g of Raney nickel. After removal of the catalyst and distillation 1.2 g of 2,5-dimethyl-4-piperidone [b.p. 78-84° (7 mm), $n^{20}D$ 1.4702; picrate, m.p. 164-165°] and 2.3 g of the original piperidone (X) were obtained.

1,2,5-Trimethyl-4-o-tolyl-4-piperidol (XI). o-Tolyllithium was prepared from 5.3 g of lithium and 53 g of o-bromotoluene in 300 ml of ether. Sixty-six g of 1,2,5-trimethyl-4-piperidone was added at room temperature. On the next day the reaction mixture, which was cooled with ice water, was treated successively with 100 ml of water, 100 ml of 18% hydrochloric acid, and 70 ml of concentrated hydrochloric acid. After treatment with sodium hydroxide the basic reaction products were extracted from the aqueous solution with ether, dried, and distilled in vacuo. There was obtained 48.5 g of a mixture of stereoisomeric piperidols (XI) [b.p. 133-135° (2.5 mm)]; on addition of benzene to the latter, 26.5 g of crystals with m.p. 105-107°, corresponding to one of the stereoisomeric forms of piperidol (XI), separated out.

Found %: N 6.24, 6.31. $C_{15}H_{23}ON$. Calculated %: N 6.01.

Picrate – m.p. 196-197° (from alcohol).

Found %: N 12.36, 12.50. $C_{21}H_{26}O_8N_4$. Calculated %: N 12.12.

The uncrystallized remainder (19.8 g) obtained after removal of the crystalline piperidol (XI), was passed through a column containing 265 g of aluminum oxide (length 1000 cm, diameter 1.8 cm). The column was washed first with chloroform (220 ml) and then with methanol (200 ml). On distillation of the chloroform 11.7 g of residue was obtained; crystallization of the latter from benzene gave an additional 1.8 g of piperidol (XI), m.p. 106-107°. The residue obtained on distillation of the methanol was a noncrystallizing , vitreous mass (6 g), which gave a picrate with m.p. 208-210°, corresponding to the other stereoisomeric form of piperidol (XI).

Found %: N 12.52, 12.57. $C_{21}H_{26}O_8N_4$. Calculated %: N 12.12.

1,2,5-Trimethyl-4-α-pyridyl-4-piperidol (XII). Butyllithium was prepared from 3.1 g of lithium and 30 g of butyl bromide in 200 ml of ether. A solution of 35 g of α-bromopyridine in 70 ml of ether was added in two portions during 5 minutes at -35°, with vigorous stirring. The stirring was continued for 15 minutes, after which 19.7 g of 1,2,5-trimethyl-4-piperidone was added at -35°. The mixture was stirred for 2 hours at room temperature, and on the next day was neutralized with 18% hydrochloric acid (to congo). The basic reaction products were separated from the water layer in the usual way and distilled in vacuo. The following fractions were obtained: 1st – 48-121° (3 mm), 10.9 g; 2nd – 121-123° (3 mm), 16.1 g – a vitreous, uncrystallizable mass. From it the dipicrate of piperidol (XII), m.p. 176-180° (from alcohol), was obtained.

Found %: N 16.88, 16.74. $C_{25}H_{26}O_{15}N_8$. Calculated %: N 16.51.

1-β-Phenylethyl-2,5-dimethyl-4-phenyl-4-piperidol (XIII). a) To the phenyllithium prepared from 0.9 g of lithium and 14 g of bromobenzene in 70 ml of ether, cooled with ice water, 10 g of 1-β-phenylethyl-2,5-dimethyl-4-piperidone (I) was added. After the reaction mixture was stirred for 2 hours at room temperature, the basic reaction products were separated out in the usual way and, after the ether was distilled off, crystallized. There was obtained 2 g of piperidol (XIII), m.p. 88-94° (from benzene).

Found %: N 4.40, 4.54. $C_{21}H_{27}ON$. Calculated %: N 4.53.

Noncrystallizing matter remaining after removal of crystals – 5.6 g.

b) A 3.3 g quantity of the γ-isomer of 2,5-dimethyl-4-phenyl-4-piperidone (m.p. 121-122°), 5 g of β-phenylethyl bromide, 2 g of calcined potash, and 8 ml of acetone were heated and stirred in a water bath for 15 hours and the acetone distilled off. The residue was neutralized with 15% hydrochloric acid (to congo).

After removal of neutral reaction products the aqueous solution was treated with potassium hydroxide. The separated bases were extracted with ether. After drying, the ether was distilled off. There was obtained 4.6 g of piperidol (XIII), m.p. 94-95° (from benzene).

Found %: N 4.66, 4.51. $C_{21}H_{27}ON$. Calculated %: N 4.53.

1-γ-Phenylallyl-2,5-dimethyl-4-phenyl-4-piperidol (XIV). An 11.5 g quantity of 1-γ-phenylallyl-2,5-dimethyl-4-piperidone (II) in 30 ml of ether was added to the phenyllithium prepared from 0.9 g of lithium and 10.4 g of bromobenzene. After the usual treatment there was obtained 12 g of basic reaction products; on crystallization of the latter from benzene 3.8 g of piperidol (XIV) was isolated in the form of colorless crystals with m.p. 145-147°.

Found %: N 4.48, 4.33. $C_{22}H_{27}ON$. Calculated %: N 4.36.

1-Nicotinoyl-2,5-dimethyl-4-phenyl-4-piperidol (XV). Six g of 2,5-dimethyl-4-phenyl-4-piperidol and 9 g of nicotinoyl chloride were heated in a water bath for 3 hours. One hundred ml of water was added to the reaction mass. The neutral products were extracted with ether, and the aqueous solution was treated with sodium bicarbonate and extracted with ether. The ether extract was dried and the ether distilled off. The residue (4.4 g), left after distilling off the ether, crystallized. There was obtained 1.5 g of piperidol (XV), m.p. 93-94° (from ether).

Found %: N 9.03, 9.10. $C_{19}H_{22}O_2N_2$. Calculated %: N 9.03.

1,2,5-Trimethyl-4-o-tolyl-4-piperidyl Propionate (XVI). To a solution of 10 g of 1,2,5-trimethyl-4-o-tolyl-4-piperidol (m.p. 105-107°) in 50 ml of benzene was added 8 g of propionyl chloride, with cooling. The mixture was heated for 8 hours in a water bath. The benzene and excess propionyl chloride were distilled off. On addition of ether the residue crystallized. There was obtained 3.6 g of the hydrochloride of propionate (XVI), m.p. 215-217° (from acetone).

Found %: N 4.72, 4.49; Cl 11.06, 11.25. $C_{18}H_{28}O_2NCl$. Calculated %: N 4.30; Cl 10.96.

1,2,5-Trimethyl-4-phenyl-4-piperidyl 3',4',5'-trimethoxybenzoate (XVII). After a mixture of 1.5 g of the α-isomer of 1,2,5-trimethyl-4-phenyl-4-piperidol (m.p. 105-107°), 3 g of trimethoxybenzoyl chloride (m.p. 80-81°), and 10 ml of benzene was refluxed for 4 hours, a crystalline mass (1.2 g) separated out. On recrystallization from acetone there was obtained 0.9 g of the trimethoxybenzoate hydrochloride of the α-isomer of 1,2,5-trimethyl-4-phenyl-4-piperidol, m.p. 182-184°.

Found %: N 3.03, 3.26. $C_{24}H_{32}O_5NCl$. Calculated %: N 3.11.

The free base, m.p. 125-126°, was obtained from the hydrochloride.

Found %: N 3.56, 3.42. $C_{24}H_{31}O_5N$. Calculated %: N 3.39.

Similarly, after a mixture of 1.5 g of the β-isomer of 1,2,5-trimethyl-4-phenyl-4-piperidol (m.p. 101-102°), 3.2 g of trimethoxybenzoyl chloride, and 15 ml of benzene was heated for 5 hours, there was obtained 2.1 g of the trimethoxybenzoate hydrochloride of the β-isomer of 1,2,5-trimethyl-4-phenyl-4-piperidol, m.p. 209-210° (from acetone).

Found %: N 3.36, 3.82. $C_{24}H_{32}O_5NCl$. Calculated %: N 3.11.

Free base – m.p. 121-122° (from benzene).

Found %: N 3.22, 3.22. $C_{24}H_{31}O_5N$. Calculated %: N 3.39.

c) From 2 g of the γ-piperidol (m.p. 106-108°) and 4.5 g of trimethoxybenzoyl chloride in 10 ml of benzene there was obtained 3.2 g of the trimethoxybenzoate hydrochloride of the γ-isomer of 1,2,5-trimethyl-4-phenyl-2-piperidol, m.p. 220-221° (from acetone).

Found %: N 3.53, 3.59. $C_{24}H_{32}O_5NCl$. Calculated %: N 3.11.

Free base – m.p. 153-154° (from benzene).

1-β-Phenylethyl-2,5-dimethyl-4-phenyl-4-piperidyl Propionate (XVIII). A mixture of 2.6 g of 1-β-phenylethyl-2,5-dimethyl-4-phenyl-4-piperidol, 1.9 g of propionyl chloride, and 15 ml of benzene was heated for

10 hours at 80°. After the benzene was distilled off, the residue was repeatedly washed with ether and then dissolved in acetone. On cooling, 1-β-phenylethyl-2,5-dimethyl-4-phenyl-4-piperidyl propionate hydrochloride (0.9 g), m.p. 169-172°, separated out.

Found %: N 3.68, 3.60. $C_{24}H_{32}O_2NCl$. Calculated %: N 3.48.

1-γ-Phenylallyl-2,5-dimethyl-4-phenyl-4-piperidyl Propionate (XIX). On refluxing 2.2 g of piperidol (XIV) and 1.7 ml of propionyl chloride in 10 ml of benzene for 7 hours there was obtained 1.4 g of 1-γ-phenylallyl-2,5-dimethyl-4-phenyl-4-piperidyl propionate hydrochloride. The hydrochloride of (XIX) consisted of colorless crystals with m.p. 110-116° (after precipitation by ether 3 times from its solution in acetone).

Found %: N 3.51, 3.31. $C_{25}H_{32}O_2NCl$. Calculated %: N 3.30.

1,2,5-Trimethyl-4-α-pyridyl-4-piperidyl Propionate (XX). To a solution of 4.9 g of 1,2,5-trimethyl-4-α-pyridyl-4-piperidol was added 16 ml of propionyl chloride at 5°. The mixture was heated in a water bath for 4 hours. After the benzene and propionyl chloride were distilled off, the residue was twice recrystallized from acetone. There was obtained 3.1 g of the dihydrochloride of propionate (XX), m.p. 129-130°.

Found %: N 7.79, 7.98. $C_{16}H_{26}O_2N_2Cl_2$. Calculated %: N 8.02.

1-Diethylaminoacetyl-2,5-dimethyl-4-phenyl-4-piperidyl Propionate (XXI). Within 15 minutes after addition of 5.5 ml of propionyl chloride to 8 g of a mixture of stereoisomeric 1-diethylaminoacetyl-2,5-dimethyl-4-phenyl-4-piperidols [b.p. 198° (2.5 mm)], dissolved in 20 ml of benzene, an oily layer was formed. The mixture was refluxed for 6 hours. The basic reaction products were then separated out in the usual way and distilled in vacuo. Two fractions were obtained: 1st – 175-190° (2.5 mm), 3.3 g; 2nd – 190-194° (2.5 mm), 2.3 g.

From 1.8 g of the 2nd fraction there was obtained 0.8 g of a mixture of the propionate hydrochlorides of stereoisomeric 1-diethylaminoacetyl-2,5-dimethyl-4-phenyl-4-piperidols, m.p. 147-159° (from acetone).

Found %: N 7.11, 7.01. $C_{22}H_{35}O_3N_2Cl$. Calculated %: N 6.82.

1-β-Phenylethyl-2,5-dimethyl-4-phenyl-4-piperidyl Phenoxyacetate (XXII). A 3.2 g quantity of piperidol (XIII), 2.1 g of phenoxyacetyl chloride, and 25 ml of benzene were refluxed for 9 hours. After the usual treatment there was obtained 1.5 g of the hydrochloride of 1-β-phenylethyl-2,5-dimethyl-4-phenyl-4-piperidyl phenoxyacetate (XXII), m.p. 200-202° (from acetone).

Found %: N 3.12, 3.20. $C_{29}H_{33}O_3N$. Calculated %: N 3.16.

1,2,5-Trimethyl-4-piperidyl β-Phenylmercaptopropionate (XXIII). A mixture of 5 g of 1,2,5-trimethyl-4-piperidol (m.p. 69-73°), 10 g of β-phenylmercaptopropionyl chloride (b.p. 139° at 4 mm), and 15 ml of benzene was heated for 8 hours. After the benzene was distilled off, the organic bases were obtained from the residue and then distilled in vacuo. Two fractions were obtained: 1st – 72-167° (2.5 mm), 2.8 g; 2nd – 167° (2.5 mm), 4.6 g.

From the 2nd fraction there was obtained 0.5 g of 1,2,5-trimethyl-4-piperidyl β-phenylmercaptopropionate hydrochloride, m.p. 76-78° (from a benzene-ether mixture).

Found %: N 3.82, 3.90. $C_{17}H_{26}O_2SNCl$. Calculated %: N 4.07.

1,2,5-Trimethyl-4-piperidyl Diethylaminoacetate (XXIV). To chloroacetyl chloride (7 ml), saturated with hydrogen chloride, was added 4.5 g of 1,2,5-trimethyl-4-piperidol (m.p. 67-71°). The mixture was heated at 80-90° for 2 hours. The excess acid chloride was distilled off. To the residue was added 25 ml of diethylamine. The mixture was refluxed for 10 hours. It was then dissolved in water and treated with soda, and the organic bases were extracted with ether. On distillation in vacuo there was obtained 7.5 g of a liquid with b.p. 88-92° (2 mm). From this, in turn, was obtained 3.4 g of 1,2,5-trimethyl-4-piperidyl diethylaminoacetate dihydrochloride, m.p. 277° (dec.) (from alcohol).

Found %: N 8.09, 8.40. $C_{14}H_{30}O_2N_2Cl_2$. Calculated %: N 8.51.

1,2,5-Trimethyl-4-piperidyl Piperidylacetate (XXV). The reaction was carried out similarly. Seven ml of chloroacetyl chloride, 4.5 g of the piperidol, and 15 ml of piperidine were taken. After the ether was distilled

off, there was obtained 6.8 g of basic reaction products, from which 0.6 g of piperidylacetate (XXV) was isolated, on crystallization from benzine, in the form of colorless crystals, readily soluble in water and difficultly soluble in benzene and benzine. M.p. 237-241°.

Found %: N 10.65, 10.80. $C_{15}H_{28}O_2N_2$. Calculated %: N 10.44.

From the remaining product there was obtained 1.5 g of the dihydrochloride of piperidylacetate (XXV), m.p. 248-251° (from an alcoholacetone mixture).

Found %: N 8.07, 8.20. $C_{15}H_{30}O_2N_2Cl_2$. Calculated %: N 8.21.

SUMMARY

A number of new γ-piperidones and γ-piperidols have been prepared. Ester hydrochlorides of certain tertiary and secondary γ-piperidols were prepared for pharmacological testing.

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SYNTHESIS OF STEREOISOMERIC 1,2,5-TRIMETHYL-4-CARBALKOXY-4-PIPERIDOLS

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In one of the reports from our laboratory [1] the synthesis of various 4-carbalkoxy-4-piperidols and the corresponding α-hydroxy acids, prepared from the cyanhydrins of 1-alkyl-2,5-dimethyl-4-piperidones, was recently described.

The acylation of these hydroxy esters by aromatic and aliphatic – aromatic acids leads to anesthetic compounds related to the analogs of the known substance α-eucaine [2] and apparently similar to dicaine in activity [3].

The cyanhydrin method, used for the synthesis of 4-carbalkoxy-4-piperidols and their esters, with all its merits has an essential shortcoming which restricts the field of its application, since it is not possible by this method to prepare stereoisomeric analogs of α-eucaine or to establish the relation between the anesthetic activity of the compounds and their steric configuration. This limitation is the consequence of the sterically directed addition of hydrogen cyanide to the carbonyl group in 1-alkyl-2,5-dimethyl-4-piperidones and the formation of only one of the four theoretically possible stereoisomeric cyanhydrins [4].

In the present paper stereoisomeric 1,2,5-trimethyl-4-carbalkoxy-4-piperidols and the corresponding hydroxy acids, obtained from stereoisomeric 1,2,5-trimethyl-4-ethynyl-4-piperidols (I) – (III), which are formed in the reaction of 1,2,5-trimethyl-4-piperidone with acetylene and were the subject of our preceding paper [5], are described.*

The advantage of the chosen route consists in the possibility of obtaining three stereoisomeric hydroxy acids (IV) – (VI), since the original acetylenic alcohols (I) – (III) are produced in the form of a mixture of three of the four theoretically possible stereoisomers, which is easily resolved.

One of the possible routes to α-hydroxy acids (IV) – (VI) of the piperidine series is oxidation of acetylenic alcohols (I) – (III) by potassium permanganate. In recent years A. I. Lebedeva and G. A. Mishnina [6], and also V. I. Nikitin and S. D. Savranskaya [7], investigated the oxidation of various tertiary acetylenic alcohols by potassium permanganate in detail and showed that the main final reaction products, as a rule, are α-hydroxy acids.

We established that the oxidation of aqueous solutions of the hydrochlorides of stereoisomeric acetylenic alcohols (I) – (III) by potassium permanganate, even in the cold, leads to the corresponding stereoisomeric 1,2,5-trimethyl-4-hydroxy-4-piperidinecarboxylic acids (IV) – (VI) which were isolated in the form of the hydrochlorides or, because of the difficulty of purification, directly converted to the methyl esters (VII) – (IX).

In contrast to compounds of the tropan series, which are usually converted by permanganate oxidation to the corresponding nor-derivatives [8], the piperidine nucleus of acetylenic alcohols (I) – (III) proved to be quite stable to the action of stoichiometric quantities of permanganate under the stated conditions, as a consequence of which additional methylation of the α-hydroxy acids formed was unnecessary.

* See scheme on p. 2262.

On oxidation of the high-melting γ-isomer of the acetylenic alcohol (III) the γ-isomer of the hydroxy acid (VI) is readily formed; the hydrochloride of the latter proved to be identical with a sample of the hydroxy acid (hydrochloride) obtained by hydrolysis of 1,2,5-trimethyl-4-cyano-4-piperidol [1]. Esterification of hydroxy acid (VI) with methanol leads to the corresponding γ-isomer of 1,2,5-trimethyl-4-carbomethoxy-4-piperidol (IX), which gave no depression in a mixture test with the sample described earlier [1]. On the basis of these results the configurative relation between the high-melting γ-isomer of the acetylenic alcohol (III) and 1,2,5-trimethyl-4-piperidone cyanhydrin, which is important in the further study of the stereochemistry of 1,2,5-trimethyl-4-piperidone derivatives, was established. Under the same conditions the low-melting α-isomer of the acetylenic alcohol (I) is oxidized to the stereoisomeric hydroxy acid (IV); the hydrochloride of the latter, which was isolated in the form of a noncrystallizing substance, was esterified with methanol, without preliminary purification, and was converted to the previously unknown α-isomer of the hydroxy ester (VII). Hydroxy acid hydrochloride (IV) is easily isolated in an analytically pure state through the hydrolysis of hydroxy ester (VII) with dilute hydrochloric acid.

Oxidation of the β-isomer of the acetylenic alcohol (II) by potassium permanganate proceeds with much greater difficulty than that of the α- and γ-isomers (I) and (III). Carrying out the reaction at elevated temperatures (up to 100°) did not lead to any increase in the yield of hydroxy acid (V). Because of the difficulty of isolating the crystalline hydrochloride of this hydroxy acid, it was also converted, without preliminary purification, to the methyl ester (VIII); by hydrolysis of the latter, the crystalline hydroxy acid hydrochloride (V) could easily be isolated.

Another possible course of synthesis of hydroxy acids (IV) – (VI) and hydroxy esters (VII) – (IX) is the oxidation of stereoisomeric 1,2,5-trimethyl-4-acetyl-4-piperidols (X) – (XII) [9]. Investigation of this variant showed that ketoalcohols (X) – (XII) are practically stable to oxidation by potassium permanganate but on treatment with bromine in alkali are easily converted to the corresponding hydroxy acids (IV) – (VI); here the use of stoichiometric quantities of sodium hypobromite is not accompanied by replacement of the methyl radical on the nitrogen atom of the piperidine ring by halogen, as occurs on treatment of piperidine [10] and compounds of the tropan series [11] with hypohalites.

Stereoisomeric hydroxy acids (IV) and (VI), obtained on oxidation of ketoalcohols (X) and (XII) with sodium hypobromite, and the corresponding methyl esters (VII) and (IX) proved to be identical with samples obtained by the permanganate oxidation of acetylenic alcohols (I) and (III).

The β-isomer of ketoalcohols (XI) is easily converted by oxidation with bromine in alkali to hydroxy acid (V); the hydrochloride of the latter, like methyl ester (VIII), corresponds exactly to the compounds obtained by oxidation of acetylenic alcohol (II) with potassium permanganate; however, higher yields can be obtained by the hypobromite method.

Because of the difficulty of purification hydroxy acids (IV) and (V) usually were not isolated, but were converted directly to the methyl esters (VII) and (VIII); after hydrolysis of the latter the crystalline hydroxy acid hydrochlorides were easily isolated. Besides hydroxy esters (VII) and (VIII), other stereoisomeric 1,2,5-trimethyl-4-carbalkoxy-4-piperidols (XIII) – (XVI), differing in the character of the alkoxy group and belonging to the α- and β-series, were also obtained from hydroxy acids (IV) and (V). Analogous hydroxy esters of the γ-series, corresponding to hydroxy acid (VI) and prepared by the cyanhydrin method, were described earlier [1].

The synthesized stereoisomeric hydroxy esters (VII) – (IX) and (XIII) – (XVI) were used for the preparation of new stereoisomeric analogs of α-eucaine.

EXPERIMENTAL

1,2,5-Trimethyl-4-hydroxy-4-piperidinecarboxylic Acid Hydrochloride (γ-isomer) (VI).

a) Oxidation of the γ-isomer of 1,2,5-trimethyl-4-ethynyl-4-piperidol (III) by potassium permanganate. Into a three-neck flask, provided with a mechanical stirrer, were put 700 ml of water, 16 ml of concentrated hydrochloric acid, and 20 g of the γ-isomer of 1,2,5-trimethyl-4-ethynyl-4-piperidol (III) [5], m.p. 177-178°. A solution of 56.8 g of potassium permanganate in 300 ml of water was added during 1 hour, the mixture being cooled to 0° and vigorously stirred; the reaction mixture was then stirred for 12 hours at room temperature. The manganese dioxide was filtered out and washed three times with portions (25 ml) of hot water. The wash waters and filtrate were combined, evaporated in vacuo to one-fourth of their original volume, acidified to congo with

concentrated hydrochloric acid, and evaporated to dryness in vacuo. After the remaining traces of water were azeotropically distilled off with benzene three times, the residue was recrystallized from anhydrous alcohol. There was obtained 20.5 g (76%) of hydroxy acid hydrochloride (VI), which after a second recrystallization from alcohol had m.p. 247-249° (dec.) and gave no depression in a mixture test with a sample described earlier [1].

b) Oxidation of the γ-isomer of 1,2,5-trimethyl-4-acetyl-4-piperidol (XII) by sodium hypobromite. Into a round-bottom, three-neck flask, provided with mechanical stirrer, reflux condenser, and dropping funnel, was put a solution of 42 g of sodium hydroxide in 350 ml of water. While the mixture was cooled to 0° and vigorously stirred, 60 g of bromine was added, and then 18.5 g of the finely-powdered γ-isomer of 1,2,5-trimethyl-4-acetyl-4-piperidol (XII), m.p. 59-60° [9], was gradually introduced during 1 hour. The mixture was stirred for 5 hours and left overnight. The separated bromoform (4.3 ml) was drawn off, and the water layer was saturated with potash, extracted several times with ether, and acidified with concentrated hydrochloric acid (to congo). When neutrality of the medium was attained, hydroxy acid (VI) was precipitated from the sodium salt, in the form of a gelatinous substance which redissolved on further acidification. The acid solution was evaporated to dryness in vacuo and the residue recrystallized from anhydrous alcohol. There was obtained 12.9 g (58%) of the easily crystallized hydroxy acid hydrochloride (VI), identical with samples obtained both in experiment "a" and by the cyanhydrin method [1].

1,2,5-Trimethyl-4-carbomethoxy-4-piperidol (γ-isomer) (IX). a) Ten g of the hydroxy acid hydrochloride (VI), obtained through the oxidation of acetylenic alcohol (III) by potassium permanganate, was dissolved in 200 ml of methanol and placed in a round-bottomed flask provided with a reflux condenser and a tube for the passage of hydrogen chloride. The reaction mixture was heated for 4 hours at 70-80° with dry hydrogen chloride continuously bubbling through, after which the methanol was distilled off at slightly reduced pressure and the residue dissolved in 50 ml of water and treated with potash. The separated base was extracted several times with ether. After drying with anhydrous magnesium sulfate and removal of the ether there was obtained 9.2 g (90%) of hydroxy ester (IX), which after recrystallization from acetone or benzine had m.p. 117-118° and gave no depression in a mixture test with a sample of the hydroxy ester, obtained by the cyanhydrin method [1].

b) A 12.9 g quantity of the hydroxy acid hydrochloride (VI), prepared through the oxidation of ketol (XII) with sodium hypobromite by the method described above, was esterified with methanol. There was obtained 9 g (87.3%) of hydroxy ester (IX), m.p. 117-118°, which proved to be identical with the sample described earlier.

1,2,5-Trimethyl-4-carbomethoxy-4-piperidol (β-isomer) (VIII). a) Oxidation of the β-isomer of 1,2,5-trimethyl-4-ethynyl-4-piperidol (II). The hydrochloride of the β-isomer of 1,2,5-trimethyl-4-hydroxy-4-piperidinecarboxylic acid (V) was prepared by oxidizing 20 g of the β-isomer of the acetylenic alcohol (II) with potassium permanganate under the conditions described above for the case of the γ-isomer (III). The oily base, obtained after the usual treatment, was distilled in vacuo: 1st fraction – 80-86° (3 mm), 10.2 g; 2nd fraction – 90-106° (3 mm), 10.1 g.

The second fraction immediately crystallized. After recrystallization from acetone the substance had m.p. 113-114° and proved to be the original acetylenic alcohol (II). The first fraction also crystallized after redistillation (80-82° at 2 mm). After recrystallization from benzine there was obtained 8 g (33%) of hydroxy ester (VIII), m.p. 70-71°.

Found %: N 7.03, 6.96. $C_{10}H_{19}O_3N$. Calculated %: N 6.96.

The hydrochloride of hydroxy ester (VIII) had m.p. 164-165° (from acetone).

Found %: N 5.93, 5.95. $C_{10}H_{20}O_3NCl$. Calculated %: N 5.89.

The methiodide of (VIII) had m.p. 154-156° (from anhydrous alcohol).

Found %: N 3.94, 4.13. $C_{11}H_{22}O_3NI$. Calculated %: N 4.08.

b) Oxidation of the β-isomer of 1,2,5-trimethyl-4-acetyl-4-piperidol (XI) with sodium hypobromite. A 22.2 g quantity of the β-isomer of 1,2,5-trimethyl-4-acetyl-4-piperidol (XI), m.p. 129-130°, was oxidized with the sodium hypobromite prepared from 72 g of bromine and 60.4 g of sodium hydroxide in 420 ml of water, under the conditions described in the experiment of oxidation of the ketol (γ-isomer) (XII). In the reaction 4.5 g of bromoform separated out.

The resulting hydroxy acid hydrochloride (V), without being isolated, was esterified with 200 ml of methanol at 75-80° for 4 hours, dry hydrogen chloride being continuously bubbled through. After the usual treatment there was obtained 12.2 g (50.6%) of the β-isomer of the hydroxy ester (VIII), b.p. 83-85° (3 mm), which crystallized completely; after recrystallization from benzine (b.p. 80-100°) it had m.p. 70-71°. The product was identical with the hydroxy ester obtained in experiment "a".

1,2,5-Trimethyl-4-hydroxy-4-piperidinecarboxylic Acid Hydrochloride (β-isomer) (V). Two g of hydroxy ester (VIII) (m.p. 70-71°) was hydrolyzed by boiling with 20 ml of dilute hydrochloric acid (1:1) for 4 hours. After the hydrochloric acid was removed in vacuo, the oily product was ground to a powder under anhydrous ether. There was obtained 1.93 g of hydroxy acid hydrochloride (V), m.p. 208-209° (from acetone).

Found %: N 6.16, 6.48. $C_9H_{18}O_3NCl$. Calculated %: N 6.26.

1,2,5-Trimethyl-4-acetyl-4-piperidol (α-isomer) (X). To a solution of 8 g of mercuric sulfate in 160 ml of water and 16 ml of concentrated sulfuric acid was added 20 g of the finely ground α-isomer of the acetylenic alcohol (I), m.p. 200-201° [5], during 1 hour with vigorous stirring. The mixture was heated for 5 hours in a boiling-water bath. The solution was neutralized with potash and treated with zinc dust. The solid matter was filtered out, and the aqueous solution was partly evaporated in vacuo and saturated with potash. The separated, oily base was extracted several times with ether and the ethereal extracts dried with anhydrous sodium sulfate. The ether was driven off and the oily residue left was distilled. There was obtained 15.4 g (83.5%) of ketol (X), b.p. 110-111° (3 mm), which quickly crystallized and, after recrystallization from benzine, had m.p. 63-64°. A mixture test with a sample of the γ-isomer of the ketoalcohol (XII) (m.p. 59-60°), obtained from the γ-isomer of the acetylenic alcohol (III), m.p. 177-178° [5], gave a depression on melting (38-43°).

Found %: N 7.88, 7.86. $C_{10}H_{19}O_2N$. Calculated %: N 7.56.

1,2,5-Trimethyl-4-carbomethoxy-4-piperidol (α-isomer) (VII)

a) Oxidation of the α-isomer of 1,2,5-trimethyl-4-ethynyl-4-piperidol (I). Ten g of the hydrochloride of 1,2,5-trimethyl-4-ethynyl-4-piperidol (α-isomer) (I), m.p. 200-201° [5], was dissolved in 800 ml of water and oxidized with 28.4 g of potassium permanganate in 200 ml of water by the method described for the β- and γ-isomers.

The resulting hydroxy acid hydrochloride (IV) was esterified with 250 ml of methanol, as described above. After the usual treatment there was obtained 5.5 g (50%) of hydroxy ester (VII), b.p. 100-110° (3 mm), which crystallized in the receiver and, after recrystallization from benzine (b.p. 80-100°), had m.p. 77-78°.

Found %: N 6.87, 6.79. $C_{10}H_{19}O_3N$. Calculated %: N 6.96.

The methiodide of hydroxy ester (VII) had m.p. 180-181° (from anhydrous alcohol).

Found %: N 4.37, 3.98. $C_{11}H_{22}O_3NI$. Calculated %: N 4.08.

The hydrochloride of (VII) had m.p. 166-167° (from acetone).

Found %: N 5.79, 5.74. $C_{10}H_{20}O_3NCl$. Calculated %: N 5.89.

b) Oxidation of the α-isomer of 1,2,5-trimethyl-4-acetyl-4-piperidol (X) by sodium hypobromite. A 4.6 g quantity of ketoalcohol (X) was oxidized with sodium hypobromite prepared from 10.5 g of sodium hydroxide, 90 ml of water, and 15 g of bromine, by the method described for the oxidation of the ketol β- and γ-isomers (XI) and (XII). In the reaction 0.9 ml of bromoform separated out. The reaction product, which was obtained after the usual treatment, was esterified with 150 ml of methanol. After working up and distillation in vacuo there was obtained 2.6 g (51.7% calculated on original ketol) of hydroxy ester (VII), m.p. 77-78°, identical with that described in the preceding experiment.

1,2,5-Trimethyl-4-hydroxy-4-piperidinecarboxylic Acid Hydrochloride (α-isomer) (IV). Two g of the hydroxy ester (VII) (m.p. 77-78°) obtained in the preceding experiment was hydrolyzed by heating with 20 ml of dilute hydrochloric acid (1:1) as described for preparation of the β-isomer of the hydroxy acid hydrochloride (V). There was obtained 1.96 g of the α-isomer of the hydroxy acid hydrochloride (IV), m.p. 195.5-196.5° (from acetone).

Found %: N 6.04, 6.03. $C_9H_{18}O_3NCl$. Calculated %: N 6.26.

1,2,5-Trimethyl-4-carbethoxy-4-piperidol (β-isomer) (XIV). Hydroxy acid hydrochloride (V) was obtained by oxidation of 25 g of ketoalcohol (XI) with sodium hypobromite prepared from 72 g of bromine, 60.4 g of sodium hydroxide, and 420 ml of water, by the method described for the preparation of hydroxy ester (VIII). After the reaction 4.5 ml of bromoform separated out. The oily product, which was obtained after the usual treatment, was esterified with anhydrous alcohol (400 ml) for 4 hours in a boiling-water bath. After the alcohol was distilled off in vacuo, the residue was dissolved in 50 ml of water and treated with potash. The oily base was extracted with ether. After removal of the ether there was obtained 12.2 g (42%) of a substance with b.p. 125-128° (2 mm), which crystallized in the receiver. After recrystallization from alcohol hydroxy ester (XIV) had m.p. 124-125°.

Found %: N 6.29, 6.19. $C_{11}H_{21}O_3N$. Calculated %: N 6.51.

1,2,5-Trimethyl-4-carbethoxy-4-piperidol (α-isomer) (XIII). Fifteen g of the hydrochloride of the α-isomer of the acetylenic alcohol (I), m.p. 200-201°, was oxidized with a solution of 41.25 g of potassium permanganate in 1500 ml of water, as described above for the preparation of hydroxy ester (VII). After the usual treatment there was obtained hydroxy acid hydrochloride (IV), which was esterified, without isolation with 250 ml of alcohol for 4 hours in a boiling-water bath, dry hydrogen chloride being bubbled through continuously. After the oily base was isolated and distilled in vacuo, there was obtained 8.7 g (45%) of hydroxy ester (XIII), b.p. 95-96° (2 mm).

Found %: N 6.82, 6.56. $C_{11}H_{21}O_3N$. Calculated %: N 6.51.

The picrate of hydroxy ester (XIII) had m.p. 141.5-142.5° (from alcohol).

Found %: N 12.46, 12.70. $C_{17}H_{24}O_{10}N_4$. Calculated %: N 12.61.

1,2,5-Trimethyl-4-carbopropoxy-4-piperidol (β-isomer) (XVI). Hydroxy acid hydrochloride (V), m.p. 208-209°, obtained by oxidizing 25 g of ketoalcohol (XI) with sodium hypobromite under the conditions described for the preparation of hydroxy ester (XIV), was esterified with propanol-1 for 3 hours at 100-110°, dry hydrogen chloride being bubbled through continuously. After the usual treatment there was isolated 12.6 g (44%, calculated on the original ketol) of a substance with b.p. 137-140° (3 mm), which crystallized in the receiver. After recrystallization from acetone, 8.8 g of hydroxy ester (XVI), m.p. 112-113°, was obtained.

Found %: N 6.02, 5.79. $C_{12}H_{23}O_3N$. Calculated %: N 6.11.

1,2,5-Trimethyl-4-carbopropoxy-4-piperidol (α-isomer (XV). Ten g of the hydrochloride of acetylenic alcohol (I) (m.p. 200-201°) was oxidized with a solution of 28.4 g of potassium permanganate in 1000 ml of water, as described for the preparation of hydroxy ester (XIII). Without purification, hydroxy acid hydrochloride (IV) was esterified for 3 hours with 250 ml of propanol-1, as described in the preceding experiment. After isolation of the base by the usual method 6.35 g (56.5%) of hydroxy ester (XV), b.p. 125-127° (2 mm), was obtained.

Found %: N 5.87, 5.95. $C_{12}H_{23}O_3N$. Calculated %: N 6.11.

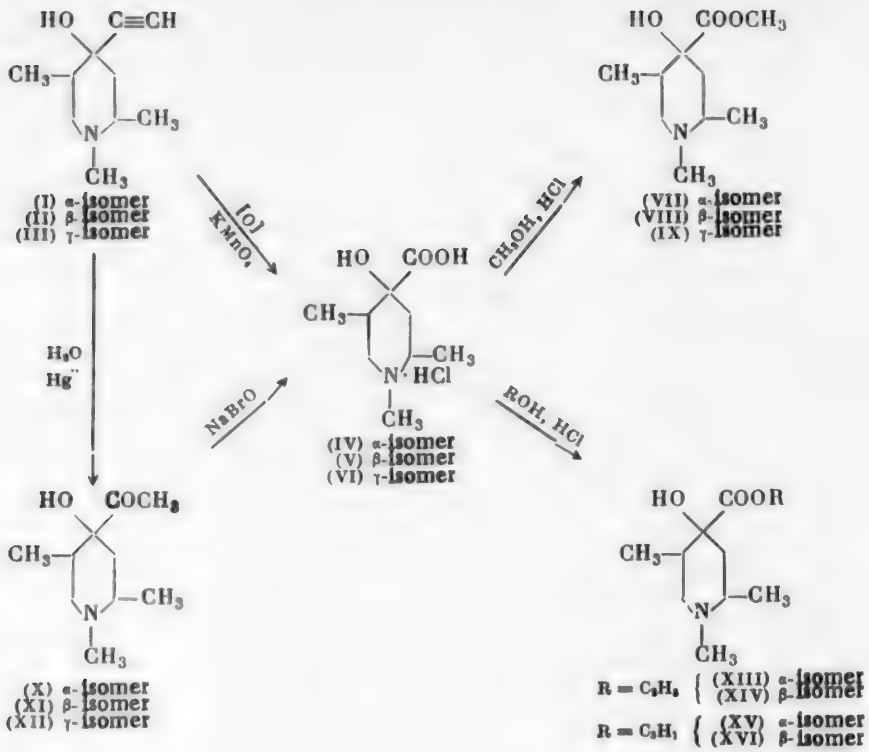
The picrate of hydroxy ester (XV) melted at 132-133° (from anhydrous alcohol).

Found %: N 12.48, 12.52. $C_{18}H_{26}O_{10}N_4$ Calculated %: N 12.22.

SUMMARY

1. The oxidation of three stereoisomeric 1,2,5-trimethyl-4-ethynyl-4-piperidols by potassium permanganate and the interaction of 1,2,5-trimethyl-4-acetyl-4-piperidols with sodium hypobromite have been described. Both methods lead to three stereoisomeric 1,2,5-trimethyl-4-hydroxy-4-piperidinecarboxylic acids and the corresponding hydroxy esters, which are intermediates in the synthesis of new anesthetic compounds. The possibility of obtaining 1,2,5-trimethyl-4-carbalkoxy-4-piperidols in the form of three stereoisomers provides, for the first time, a route toward the synthesis of previously unknown stereoisomeric analogs of α-eucaine and establishment of the relation between their anesthetic effects and steric configurations.

2. The configurative relation between the γ-isomer of 1,2,5-trimethyl-4-ethynyl-4-piperidol and 1,2,5-trimethyl-4-piperidone cyanhydrin, which is important in the study of the stereochemistry of derivatives of the 4-piperidones, has been established.



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STRUCTURE OF THE REACTION PRODUCT OF 2-AMINO-4-METHYLTHIAZOLE WITH α-OXIDES

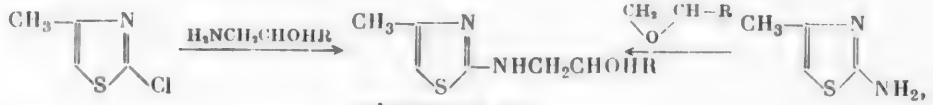
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In one of our previous papers [1], when 2-amino-4-methylthiazole was reacted with ethylene oxide, we obtained the hydroxyethyl derivative, which, based on an analogy with the behavior of 2-aminopyridine in this reaction [1, 2], was assigned the structure of N-(β-hydroxyethyl)-thiazoloneimine.

In this paper, to obtain new 2-(β-hydroxyalkyl)-aminothiazoles, and also to establish exactly the structure of the hydroxyalkyl derivatives of 2-amino-4-melhylthiazole obtained in the reaction of the latter with α-oxides, we synthesized the indicated compounds by two counter methods. The reaction of 2-chloro-4-methylthiazole with alkanolamines is a synthesis that excludes the possibility of forming nuclear nitrogen-alkylated derivatives of thiazole. It should be mentioned that using this method, B. M. Mikhailov, V. P. Bronovitskaya and I. K. Platova [3] obtained 2-(β,β'-dihydroxydiethyl)-aminothiazole when they reacted 2-bromothiazole with diethanolamine.

When 2-chloro-4-methylthiazole was reacted with ethanolamine and with 2-propanolamine we obtained 2-(β-hydroxyethyl)-amino-4-methylthiazole and 2-(β-hydroxypropyl)-amino-4-methylthiazole, respectively. A comparison of the constants of these compounds, and also of their derivatives, with the constants of the compounds obtained by us by reacting 2-amino-4-methylthiazole with the corresponding α-oxides [1], indicated that they were completely identical. This was also indisputably confirmed by the identity of the absorption spectra in the ultraviolet region of the 2-(β-hydroxyethyl)-aminothiazoles obtained by the two methods indicated above, and also by the absorption spectra in the ultraviolet region of their hydrochlorides.



where R = H, CH_3

As a result, the reaction of α-oxides with 2-amino-4-methylthiazole proceeds differently than in the case of 2-aminopyridine, and leads to the formation of 2-(β-hydroxyalkyl)-aminothiazoles, retaining the thiazole structure.

The data obtained in the present study are of special interest also for the reason that the reaction of conventional alkylating agents with 2-aminothiazoles leads to obtaining 3-alkyl-2-thiazoloneimines [4-6], whereas our described reaction of α-oxides with 2-amino-4-methylthiazole proceeds at the amino nitrogen.

EXPERIMENTAL

I. Reaction of 2-Chloro-4-methylthiazole With β-Hydroxyalkylamines

2-(β-Hydroxyethyl)-amino-4-methylthiazole. A mixture of 40 g (0.3 mole) of 2-chloro-4-methylthiazole [b.p. 161-162° (739 mm), $n^{20}D$ 1.5359, d^{20}_4 1.2944 [7], 36.5 g (0.6 mole) of ethanolamine [b.p. 78° (12 mm), $n^{20}D$ 1.4528, d^{20}_4 1.0240] and 0.3 g of copper powder was heated under reflux for 2.5-3 hours in an oil bath at 145-150°. Chloroform and saturated potassium carbonate solution were added after cooling; the chloroform layer

was separated, and the residue was extracted twice with chloroform. The extracts were combined, dried over anhydrous potassium carbonate, the chloroform distilled off, and the residue was vacuum-distilled, where the following fractions were collected: 1st, 50-173° (7 mm) – 4.6 g; 2nd, 173-185° (7 mm) – 10.8 g. Redistillation of the 2nd fraction gave a light-yellow oil:

b.p. 159-163° (5 mm), $n^{20}D$ 1.5763. Found %: N 17.85, 18.01. $C_6H_{10}ON_2S$. Calculated %: 17.71.

The picrate, prepared by mixing alcohol solutions of the free base and picric acid, had m.p. 155.5-156.5° (from alcohol).

Found %: N 17.92, 18.00. $C_{12}H_{13}O_8N_5S$. Calculated %: N 18.1.

The heating for 30 min of equimolar amounts of 2-(β-hydroxyethyl)-amino-4-methylthiazole and α-naphthyl isocyanate gave colorless crystals with m.p. 172-173° (from alcohol). The analysis data correspond to the addition product of two molecules of α-naphthyl isocyanate to one molecule of hydroxyalkylaminothiazole, therefore being both an α-naphthylurethan and an α-naphthylurea.

Found %: C 67.21, 67.17; H 5.16, 4.98; N 11.09, 11.23. $C_{28}H_{24}O_3N_4S$. Calculated %: C 67.72; H 4.87; N 11.28.

The hydrochloride of 2-(β-hydroxyethyl)-amino-4-methylthiazole was obtained by passing dry hydrogen chloride into a solution of the free base in a mixture of anhydrous alcohol and absolute ether: m.p. 143.5-144.5° (from a mixture of anhydrous alcohol and ether).

Found %: C 37.31, 37.34; H 5.51, 5.70. $C_6H_{11}ON_2SCl$. Calculated %: C 37.01; H 5.64.

2-(β-Chloroethyl)-amino-4-methylthiazole Hydrochloride. To a suspension of 3 g (0.015 mole) of 2-(β-hydroxyethyl)-amino-4-melhylthiazole hydrochloride in 15 ml of chloroform was added in drops, with stirring, 2.2 ml (0.03 mole) of thionyl chloride. After the precipitate had dissolved, the solution was heated for 30 min on the water bath, and after distilling off the chloroform the viscous oil was dissolved in anhydrous alcohol; the addition of absolute ether gave colorless crystals: m.p. 173° (from anhydrous alcohol). Yield 3.0 g (81%).

Found %: N 13.14, 13.39. $C_6H_{10}N_2SCl_2$. Calculated %: N 13.15.

2-(β-Hydroxypropyl)-amino-4-methylthiazole was obtained by the above described method. From 35 g (0.22 mole) of 2-chloro-4-methylthiazole, 32 g (0.44 mole) of β-propanolamine [b.p. 57-59° (10 mm), $n^{20}D$ 1.4442, d^{20}_4 0.9727 [8] and 0.3 g of copper powder we obtained 16.2 g (46%, based on reacted 2-chloro-4-methylthiazole) of product:

b.p. 155-159° (5 mm), $n^{20}D$ 1.5380. Found %: N 16.06, 15.98. $C_7H_{12}ON_2S$. Calculated %: N 16.28.

The hydrochloride of 2-(β-hydroxypropyl)-amino-4-methylthiazole was obtained the same as described above: m.p. 163° (from a mixture of anhydrous alcohol and ether).

Found %: N 13.13, 12.96. $C_7H_{13}ON_2SCl$. Calculated %: N 13.4.

Picrate of 2-(β-hydroxypropyl)-amino-4-methylthiazole: m.p. 151.5-152.5° (from alcohol).

Found %: N 17.30, 17.70. $C_{13}H_{15}O_8N_5S$. Calculated %: N 17.37.

The reaction of 2-(β-hydroxypropyl)-amino-4-methylthiazole with α-naphthyl isocyanate gave a compound that in its composition corresponded to the addition product of two molecules of the latter to one molecule of the hydroxy amine: m.p. 154.5-155° (from alcohol).

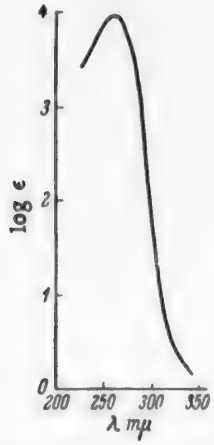
Found %: C 68.19, 68.40; H 5.15, 5.19; N 10.84, 10.82; S 6.27, 6.27. $C_{29}H_{26}O_3N_4S$. Calculated %: C 68.21; H 5.13; N 10.91; S 6.27.

II. Reaction of 2-Amino-4-methylthiazole With α-Oxides

2-(β-Hydroxyethyl)-amino-4-methylthiazole. Using the earlier described method [1], from 72 g (0.64 mole) of 2-amino-4-methylthiazole (m.p. 44°) [9] and 42 g (0.96 mole) of ethylene oxide we obtained 14.5 g of 2-(β-hydroxyethyl)-amino-4-methylthiazole:

b.p. 155-159° (4 mm), $n^{20}D$ 1.5750.

Frequency Values for 2-(β-Hydroxyethyl)-amino-4-methylthiazole (ν, cm^{-1})



Note: Tentative designations: o, i — very intense, i — intense, s — medium, m — small.

From 2-chloro-4-methylthiazole	From 2-amino-4-methylthiazole
980 i	979 i
1000 s	998 s
1063 v.i.	1064 v.i.
1133 i	1132 i
1222 v.i.	1224 i
1306 i	1304 i
1331 s	1330 s
1370 m	1370 m
1390 s	1386 s
1432 i	1430 i
1536 v.i.	1520—1550 v.i.
1646 m	1646 i
2349 i	2349 i
3098 i	3115 i
3208 i	3205 i

The picrate had m.p. 155.5-156.5°, and the mixed melting point with the picrate of 2-(β-hydroxyethyl)-amino-4-methylthiazole, obtained by the reaction of 2-chloro-4-methylthiazole with ethanolamine, was not depressed.

The hydrochloride had m.p. 144-145°, and its mixed melting point with the hydrochloride described above was not depressed.

The derivative with two molecules of α-naphthyl isocyanate had m.p. 171.5-172°, and its mixed melting point with the analogous derivative described above was not depressed.

2-(β-Hydroxypropyl)-amino-4-methylthiazole. Sixty grams (1.03 moles) of propylene oxide [b.p. 33-34° 750 mm), $n^{20}D$ 1.3670] was passed for 8 hours into a solution of 57 g (0.5 mole) of 2-amino-4-methylthiazole in 10 ml of alcohol, contained in a flask fitted with a reflux condenser and heated on the boiling-water bath. After distilling off the alcohol in vacuo the residue was distilled in a stream of nitrogen, where the following fractions were collected: 1st, 95-145° (5 mm), 37.5 g; 2nd, 145-175° (5 mm), 31.5 g; 3rd, 175-225° (5 mm), 5 g. The 1st fraction contained unchanged 2-amino-4-methylthiazole. Redistillation of the 2nd fraction gave 13.6 g of 2-(β-hydroxypropyl)-amino-4-methylthiazole with b.p. 157-161° (5 mm), $n^{20}D$ 1.5440. The picrate (from alcohol) had m.p. 152-153°, and its mixture with the previously obtained picrate of 2-(β-hydroxypropyl)-amino-4-methylthiazole had m.p. 151.5-152°. The derivative, obtained by reacting with α-naphthyl isocyanate, had m.p. 154.5-155° (from alcohol), and its mixed melting point with the earlier obtained product was not depressed.

III. Absorption Spectra*

The ultraviolet absorption spectra of the two 2-(β-hydroxyethyl)-amino-4-methylthiazole hydrochlorides described above were taken in methanol using a SF-4 spectrophotometer. Both absorption curves coincided completely when superimposed, and had λ_{max} 264 mμ and log ϵ_{max} 3.93 and 3.94 (see figure).

A single-beam IKS-11 infrared spectrometer was used to take the absorption spectra of the 2-(β-hydroxyethyl)-amino-4-methylthiazoles in the infrared region. The frequency values for the compounds, obtained from 2-chloro-4-methylthiazole and ethanolamine, and from ethylene oxide and 2-amino-4-methylthiazole, are given in the table.

SUMMARY

In contrast to the analogous reaction with 2-aminopyridine, the reaction of 2-amino-4-methylthiazole with α-oxides goes in conventional manner with the formation of a substituted amino group, i.e., without involving the cyclic-bound nitrogen atom of the thiazole nucleus in the reaction.

* We wish to thank L. A. Kazitsina for taking the absorption spectra of the compounds obtained by us.

2-(β-Hydroxyalkyl)-aminothiazoles are obtained when 2-amino-4-methylthiazole is reacted with aliphatic α-oxides. That these compounds have such a structure is confirmed by their counter synthesis via the condensation of 2-chloro-4-methylthiazole with β-hydroxyalkylamines.

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DERIVATIVES OF 2-CHROMONECARBOXYLIC ACID

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In a previous paper we described the synthesis of a number of aryl esters of 2-chromonecarboxylic acid through the chloride of this acid [1]. In most cases the chloride was prepared by reacting thionyl chloride with the acid in pyridine, and was used as such for further reaction.

In a search for pharmacologically active substances, in particular those soluble in water, we have obtained in this paper various N-substituted amides, and also some other derivatives of 2-chromonecarboxylic acid (see table).

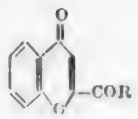
All of the compounds (I) – (XV) were synthesized by reacting 2-chromonecarboxyl chloride with the appropriate amino, hydroxy- or mercapto- derivative. The chloride, obtained in the free state by the earlier proposed method [1], was reacted in dichloroethane solution. In all except three cases (compounds (XIII) – (XV), aqueous sodium bicarbonate was used as the base to combine with the liberated hydrogen chloride. Based on the example of preparing aryl esters (XIII) – (XIV), it was shown that it is possible to acylate phenols with this chloride by the Schotten-Baumann technique.

Compounds (VIII) – (XII) give water-soluble salts when treated with either sodium bicarbonate or soda [carboxyanilide (IX)]. Hydrochloride (XV) is readily soluble in water.

Attention is attracted to the interesting relationship that exists between the color of the anilides of 2-chromonecarboxylic acid and the nature of the substituent in the benzene ring of the aromatic amine moiety. The anilide of 2-chromonecarboxylic acid is colorless [1], the p-toluidide (II) has a weak greenish-yellow color, while the p-methoxy- and p-hydroxyanilides (III) and (IV) have a yellow-green color. For the case of the p-dimethylamino- and p-diethylaminoanilides (VI) and (VII) the color now ranges from yellow-orange to red (the deeper blue color in each case is apparently due to the crystallohydrate form). The introduction of meta-orienting substituents in the para-position of the aniline moiety exerts comparatively little effect on the color. Thus, p-carboxyanilide (IX) is colorless, while p-nitroanilide (V) has only a pale yellow color. Although p-sulfoanilide (X) in the solid state is colored greenish-yellow, still in aqueous or alcohol solutions it is colorless. Its sodium salt is also colorless in the crystalline state. A similar picture is also observed for the aryl esters of 2-chromonecarboxylic acid [1]. For example, the phenyl ester is colorless, while the p-methoxyphenyl ester has a yellow color, which is less intense than for the p-methoxyanilide (III).

In all probability, the reason for the color of the substituted anilides, and also for the aryl esters of 2-chromonecarboxylic acid, is the same as for the case of the nitrobenzoyl derivatives of type $NO_2C_6H_4CONHC_6H_4R$, where R is an electron-donor group (see, for example, [2-4]). However, the final answer to this problem necessitates further studies.

At the present time it can be truthfully said only that the reason for the color of derivatives of 2-chromonecarboxylic acid cannot be attributed to the strong induction effect of the acyl radical (chromonoyl). In electrophilic characterthe 2-chromonoyl radical hardly exceeds that of the trichloroacetyl group, which to a certain degree can be confirmed by comparing the strengths of 2-chromonecarboxylic and trichloroacetic acids (the pH of a 0.1N solution in 50% alcohol is 2.55 and 2.60, respectively). In contrast to the chromonoyl radical, the trichloroacetyl radical



Compound No.	R	Empirical formula	Yield (in %)	Melting point*	Content (in %)**		
					C	H	N
I	$NHCH_2CH_2OH$	$C_{11}H_{11}O_4N$	73.9	203—204° (in water)	—	—	6.33 6.01
II	$NHC_6H_4CH_3$-p	$C_{17}H_{13}O_3N$	84.1	232—233	73.27 73.10	4.80 4.69	—
III	$NHC_6H_4OCH_3$-p	$C_{17}H_{13}O_4N$	85.7	217	—	—	4.74 4.74
IV	NHC_6H_4OH-p	$C_{16}H_{11}O_4N$	96.7	276—278	—	—	4.78 4.98
V	$NHC_6H_4NO_2$-p	$C_{16}H_{10}O_5N_2$	88.6	293—295 (from CH_3NO_2)	—	—	8.70 9.03
VI	$NHC_6H_4N(CH_3)_2$-p	$C_{18}H_{16}O_3N_2$	87.3	220—220.5	70.35 70.11	5.43 5.23	—
VII	$NHC_6H_4N(C_2H_5)_2$-p	$C_{20}H_{20}O_3N_2$	99.6	188—189	71.71 71.41	6.11 5.22	8.11 8.33
VIII	$NHCH_2COOH$	$C_{12}H_9O_5N$	82.9	223.8—227	—	—	5.50 5.67
IX	NHC_6H_4COOH-p	$C_{17}H_{11}O_5N$	93.8	353 (decomp.)	—	—	4.51 4.53
X	$NHC_6H_4SO_3H$-p	$C_{16}H_{11}O_6NS$	97.4	298 (decomp.)	—	—	4.02 4.06
XI	SCH_2COOH	$C_{12}H_8O_5S$	96.8	188—190	54.67 54.55	3.20 3.05	—
XII	4-$NHCHCH_2SH$ COOH	$C_{19}H_{11}O_5NS$	51.1	172 (decomp.)	—	—	4.67 4.78
XIII	$OC_6H_4CH_3$-p	$C_{17}H_{12}O_4$	73.1	94—95	72.98 72.84	4.46 4.32	—
XIV	$OC_6H_4NO_2$-p	$C_{16}H_9O_6N$	86.7	228—229 (from CH_3NO_2)	—	—	4.84 4.50
XV	$OCH_2CH_2N(CH_3)_2 \cdot HCl$***	$C_{14}H_{16}O_4NCl$	86.1	190—191 (from anhydrous alcohol)	—	—	5.03 4.71

has hardly any effect on the color when introduced into N,N-dimethyl-(or diethyl)-p-phenylenediamine. In addition, it is known that $p\text{-}NO_4C_6H_4CONHC_6H_4N(CH_3)_2$ is colored red [2], although the p-nitrobenzoyl group in electrophilic nature is obviously weaker than the triacetyl radical, if the reasoning is again based on the comparative strengths of the corresponding acids ($\underline{k}\ 4 \cdot 10^{-4}$ and $1.3 \cdot 10^{-1}$).

A separate communication will be made regarding the results of the pharmacological testing of the obtained compounds.

EXPERIMENTAL*

p-Toluidide (II). A solution of 2.09 g of 2-chromonecarboxyl chloride [1] in 20 ml of dichloroethane was added gradually, with stirring and ice cooling, to a mixture of 1.07 g of p-toluidine, 1.68 g of sodium bicarbonate and 5 g of water with 5 g of ice. The mixture was stirred for another 30 minutes. The precipitate was filtered washed with sodium bicarbonate solution, dilute hydrochloric acid, water, alcohol, and ether, and then dried in a vacuum desiccator over P_2O_5. The yield of toluidide (II) with m.p. 228-229° was 2.35 g (84.1%). M.p. 232-233° (from alcohol).

* With the assistance of É. K. Orlova.

Substituted anilides (III), (IV) and (V) were prepared in a similar manner (see table).

β-Hydroxyethylamide (I). For reaction, run under the conditions of the previous experiment, we took 4.18 g of 2-chromonecarboxyl chloride in 40 ml of dichloroethane, 1.47 g of monoethanolamine and 2.52 g of sodium bicarbonate in 5 ml of water with 5 g of ice. The precipitate was filtered, and washed with 10 ml of cold water, 5 ml of cold hydrochloric acid (1 : 1), and 5 ml of water. The β-hydroxyethylamide (I) was dried in a vacuum desiccator over P_2O_5. We obtained 3.45 g (73.9%) of compound with m.p. 200-201.5°.

p-Diethylaminoanilide (VII). The reaction was run in a similar manner. We took 4.6 g of the chloride in 40 ml of dichloroethane, 5.2 g of N,N-diethyl-p-phenylenediamine sulfate, and 13.6 g of $NaHCO_3$ in 50 ml of ice water. The orange precipitate was filtered and washed with sodium bicarbonate solution and water. After drying in a vacuum desiccator over P_2O_5 the compound weighed 7.05 g (99.6%, calculated as the monohydrate). Depending on the crystallization conditions, either yellow-orange or orange-red crystals (the latter are formed if conventional slow crystallization is employed) were obtained when the compound was recrystallized from alcohol. The orange-red crystals contain one mole of crystallization water, soften at 110-120°, then solidify, soften again at 160-170°, after which they solidify and melt at 188-189°.

Found %: C 67.93; H 6.37; N 7.88. $C_{20}H_{20}O_3N_2$. Calculated %: C 67.63; H 6.11; N 7.91.

If the compound is dried at 160-170° (3 mm) over P_2O_5, it melts without previous softening at 188-189° (see table).

Compound (VII) with hydrochloric and sulfuric acids gives colorless salts, which are moderately soluble in water, and suffer hydrolysis in dilute solutions. In acetone solution the reaction with dimethyl sulfate goes to completion only with a very large excess of the latter. The obtained colorless quaternary salt partially dissociates into the starting components when dissolved in acetone.

p-Dimethylaminoanilide (VI). Obtained in a similar manner, starting with 4.18 g of N,N-dimethyl-p-phenylenediamine dihydrochloride. The yellow-orange precipitate was dried at 160-170° (3 mm) over P_2O_5, after which it weighed 5.48 g (87.3%), and had m.p. 219-220°.

Depending on the crystallization conditions, recrystallization from alcohol gave either yellow-orange or dark red crystals; the latter turn yellow-orange when allowed to stand with alcohol. For analysis (see table), the compound was dried as indicated above.

Carboxymethylamide (VIII). The reaction was run the same as for the preparation of toluidide (II). We took 2.09 g of the chloride in 20 ml of dichloroethane, 1.1 g of glycine, 0.84 g of sodium bicarbonate in 20 ml of ice water and, in addition, 0.6 g of sodium hydroxide. The reaction mass was treated with 10 ml of cold hydrochloric acid (1 : 1), after which the precipitate was filtered, washed with water, alcohol and ether, and then dried in a vacuum desiccator over P_2O_5. We obtained 1.05 g (82.9%) of compound with m.p. 221-221.5°.

p-Carboxyanilide (IX) was obtained in exactly the same manner (see table).

p-Sulfoanilide (X). Reaction with 2.09 g of 2-chromonecarboxyl chloride in 20 ml of dichloroethane, 2.09 g of sulfanilic acid (dihydrate) and 2.52 g of sodium bicarbonate in 15 ml of water was run in the same manner as described for toluidide (II). The reaction mass was treated with 10 ml of conc. hydrochloric acid, after which the precipitate was filtered, dissolved in 20 ml of hot water, filtered, treated with 20 ml of conc. hydrochloric acid, and then cooled rapidly. The yellow-green precipitate was dried over KOH and P_2O_5. We obtained 3.35 g (97.4%) of compound with m.p. 295° (decomp.). To purify sulfoanilide (X) the compound was precipitated in turn from alcohol and water solution with conc. hydrochloric acid.

2-Chromonoylthioglycolic acid (XI). For reaction we took 2.09 g of the chloride in 20 ml of dichloroethane, 1.1 g of thioglycolic acid and 2.52 g of sodium bicarbonate in 30 ml of ice water. The reaction mass was treated with 10 ml of cold hydrochloric acid (1 : 1), after which the precipitate was filtered, washed thoroughly with water, and then dried in a vacuum desiccator over KOH and activated carbon. We obtained 2.5 g (96.8%) of compound with m.p. 183-185°.

N-2-Chromonoyl-1-cysteine (XII). The reaction was run the same as before. We took 8.36 g of the chloride in 80 ml of dichloroethane, 5.32 g of l-cysteine, and 10.1 g of sodium bicarbonate in 60 ml of water. At reaction end the mixture was treated with 50 ml of cold hydrochloric acid (1 : 1). The obtained viscous precipitate

crystallized when rubbed. The crystals were filtered, washed with dilute hydrochloric acid, water, 50% alcohol and ether [8.47 g, m.p. 163-164° (decomp.)], and then recrystallized from alcohol. The weight of compound (0.2 g was isolated from the mother liquor) with m.p. 170° (decomp.) was 6.0 g (51.1%). The presence of free sulfhydryl group was confirmed by reaction (in alcohol solution) with either iodine or ferric chloride.

p-Cresyl ester (XIII). A solution of 2.09 g of 2-chromonecarboxyl chloride in 20 ml of dichloroethane was added gradually, with ice cooling, to 1.08 g of p-cresol in a solution of 0.45 g of sodium hydroxide in 20 ml of water. Stirring was continued for another 30 minutes and then the dichloroethane layer was separated, washed with sodium bicarbonate, and dried over sodium sulfate. Removal of the solvent left 2.05 g (73.1%) of ester (XIII) with m.p. 90-94°.

p-Nitrophenyl ester (XIV). The reaction was run the same as before. For experiment we took 2.09 g of the chloride in 20 ml of dichloroethane, 1.39 g of p-nitrophenol, and 0.45 g of sodium hydroxide in 60 ml of water. The obtained precipitate was filtered, and washed with sodium bicarbonate solution, alcohol and ether. We obtained 2.7 g (86.7%) of ester (XIV) with m.p. 223-224°.

β-Dimethylaminoethyl ester (XV). A solution of 2.09 g of 2-chromonecarboxyl chloride in 20 ml of dichloroethane was added with cooling and stirring to 0.89 g of β-dimethylaminoethanol in 10 ml of dichloroethane. The colorless precipitate of hydrochloride (XV) was filtered, washed with a mixture (1 : 1) of anhydrous alcohol and ether, then with ether, and dried in a vacuum-desiccator over P_2O_5. We obtained 2.56 g (86.1%) of compound with m.p. 186-188°.

The hydrochloride of the β-diethylaminoethyl ester of 2-chromonecarboxylic acid was synthesized in a similar manner, yield 2.5 g (76.8%), and m.p. 186-187° (from anhydrous alcohol). From the literature [5]: m.p. 187-189°, obtained from 2-chromonecarboxylic acid and diethylaminoethyl chloride, yield not indicated.

Preparation of N-trichloroacetyl-N',N-dimethyl-p-phenylenediamine. For reaction, run in the same manner as for the synthesis of anilide (VII), we took 13.7 g of trichloroacetyl chloride in 100 ml of dichloroethane, 10.45 g of N, N-dimethyl-p-phenylenediamine dihydrochloride, and 33.6 g of sodium bicarbonate in 150 ml of water. The dichloroethane solution was separated, washed with water, and dried over sodium sulfate. After distilling off the solvent in vacuo we obtained 11.3 g (80%) of compound with m.p. 135-136°. The compound was purified by recrystallization from a mixture of petroleum ether and benzene (using carbon). Light straw-yellow needles, m.p. 136-137°.

Found %: N 10.38; Cl 38.21. $C_{10}H_{11}ON_2Cl_3$. Calculated %: N 9.97; Cl 37.86.

N-Trichloroacetyl-N',N'-diethyl-p-phenylenediamine was synthesized in a similar manner, m.p. 99.5-100°, and was obtained either as greenish granules or as nearly colorless needles.

Found %: Cl 34.56. $C_{12}H_{15}ON_2Cl_3$. Calculated %: Cl 34.37.

SUMMARY

1. The synthesis of 15 new derivatives of 2-chromonecarboxylic acid was accomplished.

2. It was found that the color of the anilides of 2-chromonecarboxylic acid depends on the nature of the substituent in the benzene ring of the aromatic amine moiety.

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SYNTHESIS AND PROPERTIES OF PYRROLIDINE BASES

VII. SOME ESTERS OF 2-METHYL-N-β-HYDROXYETHYLPYRROLIDINE

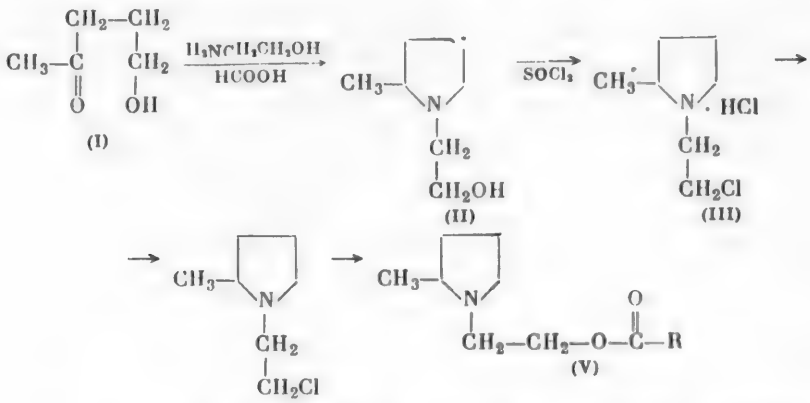
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As a continuation of our studies on the hydroamination of γ-keto alcohols [1, 2], we reacted γ-acetopropyl alcohol (I) with ethanolamine in the presence of formic acid and obtained 2-methyl-N-β-hydroxyethylpyrrolidine (II) in 56% yield.

In this paper we discuss the synthesis of 2-methyl-N-β-hydroxyethylpyrrolidine (II), and also describe some of its transformations. By reacting (II) with thionyl chloride we converted it to the hydrochloride of 2-methyl-N-β-chloroethylpyrrolidine (III), and then to the free base (IV). Reaction of (IV) with some aromatic acids led to the corresponding esters (V), which were isolated as the hydrochlorides. The esters of 2-methyl-N-β-hydroxyethylpyrrolidine were obtained in this manner, and specifically, the benzoate (Va), the o-nitrobenzoate (Vb), the p-bromobenzoate (Vc), the phenylacetate (Vd), the cinnamate (Ve), and the salicylate (Vf).



R = a) C_6H_5, b) o-$NO_2C_6H_4$, c) p-BrC_6H_4, d) $C_6H_5CH_2$, e) $C_6H_5CH{=}CH$, f) o-HOC_6H_4.

A description of the obtained esters is given in the table.

The pharmacological properties of the obtained esters were investigated at the Pharmacology Division of the Minsk Medical Institute.

All of the esters, with the exception of the phenylacetate (Vd), which was used as the methiodide, and the o-nitrobenzoate (Vb), which was used both as the hydrochloride and the methiodide, were tested as the hydrochloride. Intraveneous injection into dogs of water solutions of the indicated compounds in a disages ranging from 1 to 8 mg per kg of live weight led to a reduction of 25 to 80 mm (13 to 45% of the original value of the arterial pressure) in the blood pressure. The duration of the hypotensive effect ranged from 5 to 35 minutes for

Esters of 2-Methyl-N-β-hydroxyethylpyrrolidine

R	Formula	Solvent	Melting point	Yield (in %)	Found (%)		Calculated (%)	
					C	H	C	H
(Va) C_6H_5	$C_{15}H_{22}O_2NJ$ Methiodide	Butanol — ether	157—158°	56	47.56, 47.39	6.16, 6.64	48.01	5.91
(Vb) o-$NO_2C_6H_4$	$C_{14}H_{19}O_4N_2Cl$ Hydrochloride	Ethyl acetate + alcohol	175—180	91	53.12, 53.08	5.92, 5.78	53.42	6.08
(Vc) n-BrC_6H_4	$C_{14}H_{19}O_2NClBr$ Hydrochloride	Acetone + alcohol	183—184	72	50.01, 49.93	5.35, 5.48	50.25	5.72
(Vd) $C_6H_5CH_2$	$C_{16}H_{24}O_2NJ$ Methiodide	Isopropyl alcohol	128—129	84	49.15, 49.22	6.28, 6.32	49.30	6.21
(Ve) C_6H_5CH-CH	$C_{16}H_{22}O_2NCl$ Hydrochloride	Acetone + alcohol	178—180	94	64.84, 64.97	7.61, 7.50	64.36	7.50
(Vf) HOC_6H_4	$C_{14}H_{20}O_3NCl$ Hydrochloride	Acetone + alcohol + ether	134—135	80	58.56, 58.83	7.13, 7.06	58.76	7.05

the different preparations. The introduction of various substituents in the ortho and para positions of the benzene ring was essentially without effect on the hypotensive activity.

Special analysis revealed that the hypotensive action exerted by the investigated compounds is based on their ability to terminate in the vicinity of the vegetative nodes the transmission of nerve impulses to the blood vessels (ganglion-blocking effect). An exception is the cinnamate (Ve), which, being essentially devoid of ganglion-blocking activity, lowers the blood pressure by direct weakening effect on the smooth muscles of the blood vessels (an action similar to that exerted by papaverine).

The methiodide of the o-nitrobenzoate (Vb), and especially the methiodide of the phenylacetate (Vd) and the cinnamate (Ve), exhibit the property of preventing a reduction in the blood pressure of dogs after the injection of acetylcholine (atropinelike effect). This atropinelike effect is observed when the indicated compounds are injected in doses of 1-2.5 mg/kg, and lasts for 10-20 minutes.

The p-bromobenzoate (Vc), salicylate (Vf) and cinnamate (Ve) exhibit local anesthetic action (anesthetizing the cornea of rabbits), in which connection the activity of their 5% solutions is less than the activity of a 5% novocaine solution by a matter of 12, 11 and 7 times, respectively (the testing was done by N. A. Iskarev).

In its pharmacological properties the hydrochloride of the cinnamate (Ve) is similar to the domestic benzacine (hydrochloride of the dimethylaminoethyl ester of benzilic acid) and to the foreign benactizane (hydrochloride of the diethylaminoethyl ester of benzilic acid), both of which find clinical use as spasmolytic (hypotensive) agents and as tranquillizers, removing the symptoms of fear and anxiety in neurotic cases [3-5].

EXPERIMENTAL

We started with technical γ-acetopropyl alcohol (I), which after purification had the following constants:

B.p. 114-115° (30 mm), $n^{20}D$ 1.4395, d_4^{20} 1.0068, MR_D 26.69.

Literature [6]: B.p. 115-116° (30 mm); MR_D 1.4350.

2-Methyl-N-β-hydroxyethylpyrrolidine (II). Into a distillation flask, fitted with thermometer, descending into the liquid, and a receiver, was charged

20.2 g of γ-acetopropyl alcohol, 30.6 g of ethanolamine, 10 ml of 85% formic acid, and 2 g of powdered nickel (from nickel formate). Reaction began at 110° and proceeded with the copious evolution of CO_2. As the stream of evolved CO_2 subsided, two 15 ml portions of formic acid were added and the temperature was gradually raised to 160°. The reaction was stopped after 16 hours. The reaction mixture was hydrolyzed by heating for 2 hours with 100 ml of hydrochloric acid, then neutralized with 40% NaOH solution, extracted with ether, and fractionated in vacuo. We obtained 14 g (56%) of (II).

B.p. 70-71° (6 mm), $n^{20}D$ 1.4700, d_4^{20} 0.9582, MR_D 37.64. $C_7H_{15}ON$. Calculated 37.73.

Literature [7]: B.p. 72° (8 mm), $n^{20}D$ 1.4683.

2-Methyl-N-β-chloroethylpyrrolidine (IV) and Hydrochloride (III). The method described for the synthesis of N-β-chloroethylpyrrolidine was used [8]. A charge of 51 g of 2-methyl-N-β-hydroxyethylpyrrolidine (II) in 150 ml of chloroform was placed in a three-necked flask. The flask was cooled in an ice-salt mixture, and then, with vigorous stirring, 60 g of thionyl chloride was added slowly from a dropping funnel. After standing for 12 hours the reaction mixture was treated with 20 ml of anhydrous methanol and the whole evaporated in vacuo. The residue crystallized when triturated with an ethyl acetate-ether mixture (1:1). Recrystallization gave 67 g (93%) of hydrochloride (III), which was dissolved in 30 ml of water and then made alkaline with saturated potassium carbonate solution. The floating oil was extracted with ether, dried, and fractionated in vacuo. We obtained 49 g of free base (IV).

B.p. 59-60° (8 mm), $n^{20}D$ 1.4655, d_4^{20} 0.9874, MR 41.09. $C_7H_{14}NCl$ Calculated 41.13.

Literature [9]: B.p. 60-62° (8 mm), $n^{20}D$ 1.4622.

2-Methyl-N-β-hydroxyethylpyrrolidine Benzoate (Va) Hydrochloride. To prepare the esters of 2-methyl-N-hydroxyethylpyrrolidine, we used the method described by Horenstein and Pählicks [10] to prepare the esters of aliphatic amino alcohols.

A mixture, composed of 7.5 g of free base (IV) and 6.1 g of benzoic acid, was dissolved in 35 ml of alcohol, after which the solution was evaporated in vacuo at 45°. The residue was kept for 2 hours at 55°, and after it had solidified it was ground well and again heated at 90° for 5 hours. The reaction mass was dissolved in butanol, filtered from insoluble material, and then precipitated with ether. Here (Va) crystallized gradually.

We obtained 7.8 g (56%) of (Va). Methiodide, m.p. 157-158° (from benzene).

Found %: C 47.56, 43.39; H 6.16, 6.04. $C_{15}H_{22}O_2NI$. Calculated %: C 48.01; H 5.91.

SUMMARY

1. The reaction of γ-acetopropyl alcohol with ethanolamine in the presence of formic acid gave a 56% yield of 2-methyl-N-β-hydroxyethylpyrrolidine.

2. A number of esters of 2-methyl-N-β-hydroxyethylpyrrolidine were synthesized, and specifically the following: benzoate, o-nitrobenzoate, p-bromobenzoate, phenylacetate, cinnamate, and salicylate.

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SYNTHESES USING ACRYLONITRILE

XXXIII. CYANOETHYLATION OF p-CRESOL

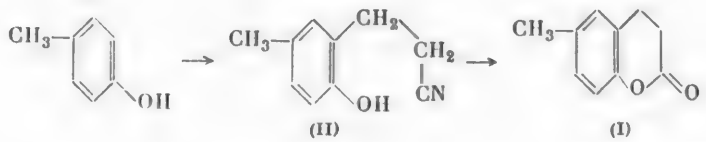
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Cyanoethylation of the benzene ring proceeds under comparatively drastic conditions and with a low yield (in the presence of aluminum chloride), but replacing the acrylonitrile by β-chloropropionitrile permits raising the yield several fold [1]. With phenols the matter is more complicated. In alkaline medium acrylonitrile adds to the hydroxyl group with the formation of β-aryloxypropionitriles, but in the case of phenols, capable of yielding tautomeric derivatives, cyanoethylation under such conditions proceeds with transfer of the reaction center to the ortho position of the benzene ring [2, 3]. In the presence of aluminum chloride, phenol cyanoethylates in the para position, giving a small amount of the ortho isomer as impurity, which during reaction suffers cyclization with the formation of dihydrocoumarin [2, 4]. If the para position is occupied by an alkyl group, then, according to the patent literature [2], reaction is in the ortho position, but in small yield. Polyhydric phenols (resorcinol, orcinol, phloroglucinol) under these conditions form dihydrocoumarins in good yields [2, 5].

We were interested in the possibility of synthesizing 6-alkylcoumarins from the corresponding p-alkylphenols and acrylonitrile. In connection with this we undertook a study of the conditions for the reaction of p-cresol with acrylonitrile in the presence of aluminum chloride.

It proved that the reaction fails to go at low temperatures (below 10°). We also found that the reaction could not be run in carbon tetrachloride as the solvent. Profound tarring occurs when the reaction is run in nitrobenzene in the presence of aluminum chloride. Without solvent (an equimolar mixture of p-cresol and acrylonitrile was first saturated with hydrogen chloride and then an equimolar amount of aluminum chloride was added), in 1 hour at 80°, the reaction went only to the extent of 16%, in which connection half of the product was isolated as 6-methyl-3,4-dihydrocoumarin (I). The other half, the fraction with b.p. 128-133° (10 mm), was a mixture of approximately equal amounts of dihydrocoumarin (I) and, apparently, nitrile (II). However, we were unable to isolate the latter in sufficiently pure form.



(II) (I)

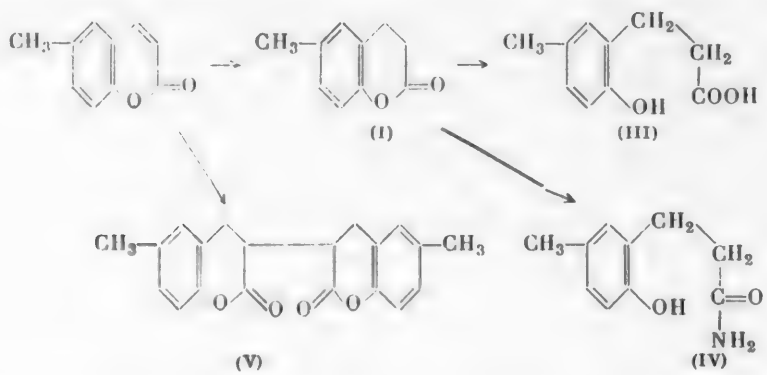
If the reaction is run for a longer time (9 hours, 100°), and either the amount of acrylonitrile or aluminum chloride is increased, then the total yield fails to suffer essential change, but nearly all of the β-(2-hydroxy-5-methylphenyl)propionitrile (II) cyclizes. Conversely, short heating at 200° gave only a liquid fraction with b.p. 128-133° (10 mm). As a result, increasing the reaction time leads to the predominant formation of lactone (I).

If the acrylonitrile is replaced by β-chloropropionitrile, then with an equivalent ratio of the components (6 hours, 95-130°) the total yield of mixture (I) and (II) does not exceed 11%. However, if p-cresol, β-chloropropionitrile and aluminum chloride are taken in the molar ratio 1 : 5 : 3, and the heating is for 3 hours at 95-115° and for 7.5 hours at 120-140°, then the yield of nitrile (II) is 4.3%, and that of lactone (I) is 41.4%. Increasing

the reaction time to 30 hours causes both the yield and the ratio of the reaction products to change slightly [3.4% of (II) and 45.4% of (I)]. The 6-methyl-3,4-dihydrocoumarin (I) obtained in the manner indicated above had m.p. 79.0-79.5°, which is not in agreement with the data given in the literature.

In 1925 Thompson and Edee [6] indicated that the heating of p-cresol with succinic acid (in the presence of sulfuric acid) gave a substance with m.p. 71-72°, the structure of which was not proved, but which was postulated to be lactone (I). When this experiment was repeated we failed to obtain the indicated substance (instead the original cresol and succinic acid were isolated). The same paper [6] also describes the reduction of an alcohol solution of 6-methylcoumarin with 30% sodium amalgam, in which connection the isolated substance with m.p. 225° was more reliably assigned the structure of 6-methyl-3,4-dihydrocoumarin. However, it is known that only in dilute solutions does the reduction of coumarins with sodium amalgam go smoothly with the addition of 2 atoms of hydrogen and the simultaneous cleavage of the lactone ring [7], whereas in concentrated solutions there also occurs a doubling of the molecules, so that the obtained acids on lactonization form bis-dihydrocoumarins [8]. The latter have melting points above 200°, whereas the dihydrocoumarins melt below 100° [9].

Our compound (I) shows the typical properties of a 3,4-dihydrocoumarin. It fails to titrate in the cold with 0.1N alkali solution, but when heated it suffers cleavage of the ring, giving the salt of 5-methylmelilotic acid (III). Also, reaction of (I) with alcoholic ammonia solution readily gives the amide of this acid (IV). When 6-methylcoumarin was reduced with 4% sodium amalgam (in dilute solution) we obtained a compound with m.p. 78.5-79.0° and a molecular weight of 156.2, which corresponded to the monomer, and proved to be identical with the (I) obtained in the cyanoethylation of p-cresol. As a result, the structure of the obtained lactone (I) was proved. At the same time we isolated 10 mg of a substance with m.p. 225-226°, proving to be identical with that described earlier [6], and apparently having the structure of bis-dihydrocoumarin (V).



An attempt to repeat the experiment (see [6]) on the reduction of a more concentrated solution of 6-methylcoumarin in aqueous alcohol with 30% sodium amalgam for the purpose of obtaining a larger quantity of (V) proved unsuccessful. Only lactone (I) was obtained under the conditions used by us. An apparent explanation for this is that the experimental details (amount of alcohol, temperature, reaction time, pH of the medium), omitted in the paper by Thompson and Edee, exert a decisive influence on the course of the reaction. At the present time it is known (see, for example, [10]) that the reductive dimerization of α,β-unsaturated acids and their derivatives when reacted with metal (Li, K, Na) amalgams is a general phenomenon. Reductive dimerization and ordinary hydrogenation of the double bond are concurrent reactions, in which connection the optimum conditions for progress of the former are as follows: absence of alcohol, acid medium, and lithium amalgam. For the alkali metal amalgams the reactivity (with respect to reductive dimerization) increases from sodium amalgam to lithium amalgam. In view of the fact that we ran our reaction in alkaline medium, in the presence of a substantial amount of alcohol, and used sodium amalgam, reductive dimerization practically did not occur, in which connection the use of 4% sodium amalgam, due to the lower alkalinity of the medium and the smaller amount of alcohol present, gave a small amount of (V), whereas with 30% sodium amalgam it was not obtained at all.

EXPERIMENTAL

Cyanoethylation of p-Cresol. Into a three-necked flask, fitted with a stirrer, reflux condenser, thermometer, and protected with a calcium chloride tube, was charged 10.8 g of p-cresol and 44.8 g of β-chloropropionitrile, and then 40 g of freshly sublimed anhydrous aluminum chloride was added in small portions, maintaining the temperature in the flask at about 20° (ice cooling). After heating (3 hr at 95-115°, 7 hr at 120-130°, and 0.5 hr at 140°), the mixture was cooled to room temperature and then poured into a mixture of ice and hydrochloric acid. The whole was then extracted several times with ether, the extracts dried over magnesium sulfate, the ether distilled off, and the residue was vacuum-distilled. Unreacted β-chloropropionitrile and p-cresol (38.1 g) came over at the start, and then the following two fractions were collected: 1st, 1.4 g, greenish liquid with b.p. 128-133° (10 mm), $n^{20}D$ 1.5345, d_4^{20} 1.1563; 2nd, 6 g (37%), b.p. 150-155° (10 mm), m.p. 70-73°. Several recrystallizations from aqueous alcohol and octane gave 6-methyl-3,4-dihydrocoumarin (I) as prismatic crystals with m.p. 79.0-79.5°.

Found %: C 73.85, 73.91; H 6.34, 6.43. $C_{10}H_{10}O_2$. Calculated %: C 74.05; H 6.22.

The compound is readily soluble in alcohol, ether, chloroform and carbon tetrachloride, moderately soluble in n-octane, and difficulty soluble in petroleum ether and in boiling water. In the cold it is insoluble in 1N sodium carbonate and sodium hydroxide solutions, but it gradually dissolves in 30% NaOH solution. Lactone (I) must be kept in sealed ampuls, since on standing in the air it suffers partial cleavage of the lactone ring with the formation of 5-methylmelilotic acid, which was shown by titration with 0.1N alkali solution, and from the elementary analysis data (decrease in the C percent and increase in the H content).

The 1st fraction with b.p. 128-133° (10 mm) contained approximately equal amounts of lactone (I) (isolated by freezing out; after recrystallization it proved to be identical with the above described 6-methyl-3,4-dihydrocoumarin) and a greenish liquid, from which traces of lactone (I) were removed by shaking for 10 minutes with 25% alcoholic ammonia solution. After redistillation, nitrile (II) had the following constants:

B.p. 130-132° (10 mm), $n^{20}D$ 1.5440, d_4^{20} 1.1138, MR_D 46.69; calc. 46.12.

In a similar experiment, from 10.8 g of p-cresol and 9.8 g of acrylonitrile (previously saturated with dry HCl) and 18.7 g of aluminum chloride, after heating (2.5 hr at 120-130° and 5 min at 200°), decomposition, and distillation, we isolated only 4.63 g of a fraction with b.p. 128-133° (10 mm).

β-(5-Methyl-2-hydroxyphenyl)propionic Acid (III). To a solution of 1.22 g of lactone (I) in 18 ml of alcohol was added 18 ml of 10% aqueous sodium hydroxide solution, the whole refluxed for 2 hr, then cooled, extracted several times with ether, the water solution acidified with 20% sulfuric acid, and the separated acid (III) again extracted with ether. For purification the acid was extracted from the ether with 3% sodium carbonate solution, the carbonate solution acidified, the acid again extracted with ether, and the ether evaporated. After drying in vacuo we obtained 1.37 g (100%) of acid (III) as prismatic crystals. M.p. 83.5-84° [from a mixture of benzine and benzene (2:1)].

Found %: C 66.72, 66.83; H 6.74, 6.88. M 180.6. $C_{10}H_{12}O_3$. Calculated %: C 66.64; H 6.65; M 180.2.

The compound is readily soluble in ether and alcohol, and moderately soluble in cold water. It gives a yellow-green color with ferric chloride solution.

β-(5-Methyl-2-hydroxyphenyl)propionamide (IV). To a solution of 3.25 g of 6-methyl-3,4-dihydrocoumarin (I) in 6.5 ml of alcohol was added 20 ml of concentrated aqueous ammonia solution, and the whole was shaken on a shaker for 10 minutes. The reaction mixture was transferred to a crystallizing dish, where the ammonia was allowed to evaporate freely (for 3 hours), and here handsome colorless plate crystals of amide (IV) deposited, which were washed with water, then with benzene (after drying on the filter), and dried in a vacuum oven. The yield was quantitative, m.p. 113-113.5° (from either water or benzene).

Found %: C 67.07, 67.13; H 7.43, 7.52; N 7.79, 7.85. $C_{10}H_{13}O_2N$. Calculated %: C 67.07; H 7.31; N 7.82.

Amide (IV) is readily soluble in hot water, moderately soluble in boiling benzene, and practically insoluble in ether and cold water. Its water solution shows neutral to litmus, and it gives a green color with aqueous ferric chloride solution.

Reduction of 6-Methylcoumarin

6-Methylcoumarin was synthesized from p-cresol and maleic acid [6], and was purified either by recrystallization from aqueous alcohol, followed by chromatographing on aluminum oxide and then elution with a mixture of benzene and petroleum ether, or by 2-fold fractional distillation in vacuo. In both cases the purified compound had m.p. 71.5-72.0°. Literature: m.p. 71-72° [6], and 73-74° [11].

The obtained 6-methylcoumarin fails to react in the cold with alcoholic ammonia solution.

Reduction of 6-Methylcoumarin With 4% Sodium Amalgam. To a solution of 0.5 g of 6-methylcoumarin in 70 ml of alcohol was added 140 ml of water, and then 12.5 g of 4% sodium amalgam was added gradually (in 6 hr) in small portions, maintaining the temperature of the mixture between 40 and 60°. After cooling, the mixture was acidified with 20% sulfuric acid, extracted 3 times with ether, and the combined ether extract washed several times with 3% aqueous sodium carbonate solution. Evaporation of the ether left 0.02 g of unreacted 6-methylcoumarin with m.p. 71.5-72.0°. The sodium carbonate extracts were acidified, extracted with ether, the ether distilled off, and after drying in a vacuum we obtained 0.54 g (96%) of acid (III) with m.p. 83.5-84° (from a mixture of gasoline and benzene). The mixed melting point with the above described 5-methylmelilotic acid was not depressed. Vacuum distillation of acid (III) gave lactone (I) with b.p. 140-142° (8 mm), and m.p. 78.5-79.0° (from n-octane). Its mixed melting point with the (I) obtained in the cyanoethylation of p-cresol was not depressed. Treatment with alcoholic ammonia solution gave the amide with m.p. 113-113.5°, which failed to depress the melting point when mixed with the amide (IV) described above. Cryoscopic determination (in benzene) of the molecular weight of lactone (I) gave a value of 156.2 ($C_{10}H_{10}O_2$. Calculated 162.2). The residue in the flask from the distillation of lactone (I) was recrystallized from alcohol and gave 10 mg of substance with m.p. 225-226° [6].

Reduction of 6-Methylcoumarin With 30% Sodium Amalgam. To a solution of 3.5 g of 6-methylcoumarin in 100 ml of alcohol and 40 ml of water, in a CO_2 atmosphere, was added 70 g of 30% sodium amalgam in 3 hours. The reaction mixture was heated for 5.5 hours at 80°, and then allowed to stand for a day at room temperature. After working up as described above we isolated 1.03 g of starting 6-methylcoumarin and 2.45 g (62.3%) of acid (III) with m.p. 83.5-84°, from which we obtained lactone (I) with m.p. 79.0-79.5° on vacuum distillation.

SUMMARY

The conditions for the nuclear cyanoethylation of p-cresol were studied. The synthesis of 5-methylmelilotic acid and its derivatives, including 6-methyl-3,4-dihydrocoumarin, was described.

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SYNTHESIS OF 2,6,10,14,18,22-HEXAMETHYL-2,6,10,14,18,23-TETRACOSAHEXAEN-22-OL – FARNESYLNEROLIDOL

G. A. Vorob'eva, I. K. Sarycheva and N. A. Preobrazhenskii

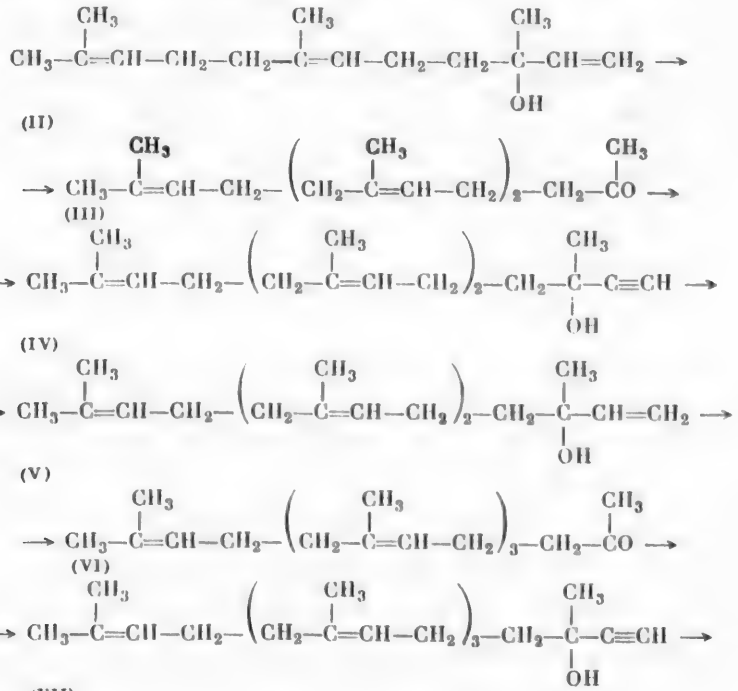
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Besides rubber and gutta, natural-occurring compounds of the terpene series, or isoprene polymers, also include farnesylfarnesol, $C_{30}H_{50}O$, the main constituent of β-phylloquinone (vitamin K_2 group) [1], solanesol [2], $C_{30}H_{50}O$, and other polyterpenes.

The presence of double bonds and methyl groups determines the geometric isomerism of these compounds, with which both their physicochemical and biological properties are linked. Cis-trans isomerism creates a number of difficulties in accomplishing a stereospecific synthesis of such isoprenoid compounds, since interconversions of stereo structures are frequently observed in the course of the chemical reactions involved, leading to a mixture of isomers.

In this paper we describe the synthesis of 2,6,10,14,18,22-hexamethyl-2,6,10,14,18,23-tetracosahexaen-22-ol, or farnesylnerolidol (I), by the condensation of β,γ-unsaturated alcohols with acetoacetic ester [3].

The starting material for the desired synthesis was 2,6,10-trimethyl-2,6,11-dodecatrien-10-ol, or nerolidol (II) [4]. The successive creation of the isoprenoid linkages present in farnesylnerolidol (I) was accomplished by the use of three monotypical methods, including the synthesis of ketones using either acetoacetic ester or diketene, condensation with acetylene, and selective hydrogenation.



(II)

(III)

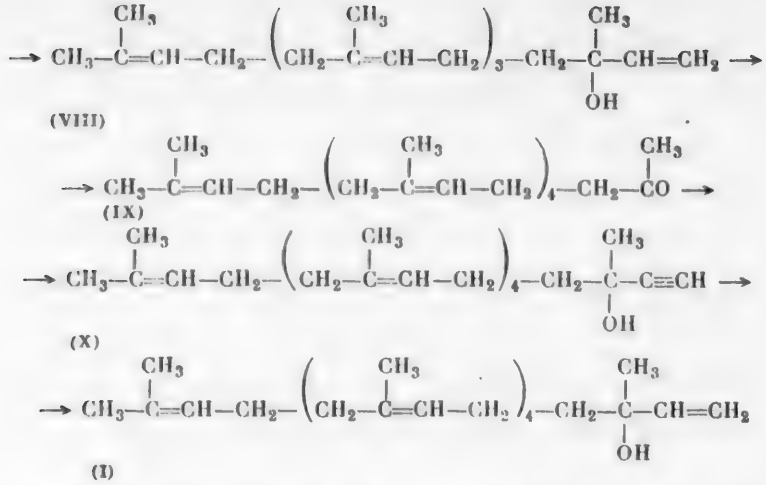
(IV)

(V)

(VI)

(VII)

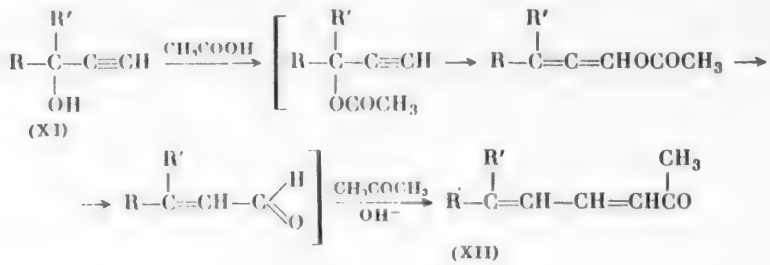
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2,6,10-Trimethyl-2,6,11-dodecatrien-10-ol (II) was reacted with acetoacetic ester. Condensation of the thus obtained 2,6,10-trimethyl-2,6,10-pentadecatrien-14-one (III) with sodium acetylide gave 2,6,10,14-tetramethyl-2,6,10-hexadecatrien-15-yn-14-ol (IV), which was selectively hydrogenated in the presence of palladium catalyst [4] to 2,6,10,14-tetramethyl-2,6,10,15-hexadecatetraen-14-ol (V). Alcohol (V) was subjected to an analogous cycle of transformations. Here 2,6,10,14-tetramethyl-2,6,10,14-nonadecatetraen-18-one (VI), 2,6,10,14,18-pentamethyl-2,6,10,14-eicosatetraen-19-yn-18-ol (VII) and 2,6,10,14,18-pentamethyl-2,6,10,14,19-eicosapentaen-18-ol (VIII) were synthesized in succession. The transition from (VIII) to farnesylnerolidol (I) included the stages of synthesizing 2,6,10,14,18-pentamethyl-2,6,10,14,18-tricosapentaen-22-one (IX) and 2,6,10,14,18,22-hexamethyl-2,6,10,14,18-tetracosapentaen-23-yn-22-ol (X).

EXPERIMENTAL

2,6,10-Trimethyl-2,6,11-dodecatrien-10-ol (II) (b.p. 113-114° at 3 mm, d_4^{20} 0.8782, $n^{20}D$ 1.4780, MR_D 71.69; calc. 71.59) was obtained by us from 2-methyl-3-butyn-2-ol [(XI), R = R' = CH_3] (b.p. 43-45° at 85 mm) via 2-methyl-2,4-heptadien-6-one [(XII), R = R' = CH_3] (b.p. 85-86° at 10 mm, $n^{20}D$ 1.5290, λ_{max} 290 mμ, ε 27600) and then by an analogous method using the scheme described in [5], worked out for the given case by G. I. Samokhvalov, L. V. Vakulova and one of the authors of the present paper.



2,6,10-Trimethyl-2,6,10-pentadecatrien-14-one (III). A mixture of 90 g of nerolidol (II) and 200 g of acetoacetic ester was heated in a stream of nitrogen at 155-160° for 55 hours. Then the excess acetoacetic ester was distilled from the reaction mass, and the residue was fractionally distilled. Yield 69.2 g (65.16%).

B.p. 120-121° (0.45 mm), d_4^{20} 0.8835, $n^{20}D$ 1.4811, MR_D 84.53; calc. 83.93.

Found %: C 82.80; H 11.31. $C_{18}H_{30}O$. Calculated %: C 82.39; H 11.53.

IR-Spectrum: 3400 (very weak), 2900 (very strong), 1720 (very strong), 1465 (very strong), 1430 (very weak), 1395 (strong), 1220 (weak), 1165 (medium), 1125 (very weak), 1085 (very weak), 840 (weak), 805 (weak), 740 (weak) cm^{-1}.

2,6,10,14-Tetramethyl-2,6,10-hexadecatrien-15-yn-14-ol (IV). A solution of 105 g of 2,6,10-trimethyl-2,6,10-pentadecatrien-14-one (III) in 100 ml of absolute ether was added in 1 hour to sodium acetylide, previously prepared from 20.1 g of sodium and dry acetylene in 500 ml of liquid ammonia. The reaction mixture was stirred for 3 hours, and then allowed to stand for 24 hours at 18-19°. The obtained thick dark yellow mass was treated with 250 ml of ice water and then acidified with 100 ml of sulfuric acid (d 1.395) to pH 6.5. The obtained upper layer was separated, while the reaction product in the lower layer was extracted with 300 ml of ether. The combined ether extracts were dried over sodium sulfate. The residue after removal of the solvent was distilled. Yield 70 g (60.68%).

B.p. 138-139° (0.65 mm); d_4^{20} 0.8790, $n^{20}D$ 1.4850, MR_D 94.01; calc. 92.62.

Found %: C 83.46; H 11.30. $C_{20}H_{32}O$. Calculated %: C 83.26; H 11.18.

2,6,10,14-Tetramethyl-2,6,10,15-hexadecatetraen-14-ol (V). Ten grams of 2,6,10,14-tetramethyl-2,6,10-hexadecatrien-15-yn-14-ol (IV) in 40 ml of petroleum ether (b.p. 80-105°) was hydrogenated at 19° and 760 mm in the presence of 1 g of palladium catalyst and 0.1 g of quinoline, with mechanical agitation. The hydrogenation practically ceased after 770 ml of hydrogen had been absorbed. The catalyst was filtered and washed with 40 ml of ether. The combined filtrates were washed in succession with sulfuric acid (d 1.032) and sodium bicarbonate solution, and then dried over sodium sulfate. The residue after distilling off the solvent was fractionally distilled. Yield 9.6 g (89.9%).

B.p. 115-116° (0.3 mm), d_4^{20} 0.8744, $n^{20}D$ 1.4820, MR_D 94.69; calc. 94.22.

Found %: C 82.77, 82.78; H 11.56, 11.67. $C_{20}H_{34}O$. Calculated %: C 82.69; H 11.80.

IR-spectrum: 3400 (medium), 2900 (very strong), 1715 (strong), 1660 (weak), 1460 (strong), 1390 (strong), 1295 (weak), 1260 (weak), 1175 (medium), 1125 (medium), 1000 (weak), 920 (weak), 820 (weak) cm^{-1}.

2,6,10,14-Tetramethyl-2,6,10,14-nonadecatetraen-18-one (VI). A mixture of 28 g of 2,6,10,14-tetramethyl-2,6,10,15-hexadecatetraen-14-ol (V) and 50 g of acetoacetic ester was heated in a stream of nitrogen at 160-165° for 55 hours. The yield of ketone (VI) was 15 g (47.1%).

B.p. 122-124° (0.25 mm), d_4^{20} 0.8826, $n^{20}D$ 1.4828, MR_D 106.9; calc. 106.56.

Found %: C 83.20, 83.33; H 11.51, 11.41. $C_{23}H_{38}O$. Calculated %: C 83.58; H 11.60.

IR-spectrum: 3400 (strong), 2900 (very strong), 1715 (very strong), 1465 (strong), 1390 (weak), 1275 (weak), 1180 (weak), 900 (weak), 840 (weak), 765 (weak) cm^{-1}.

2,6,10,14,18-Pentamethyl-2,6,10,14-eicosatetraen-19-yn-18-ol (VII). A solution of 15 g of 2,6,10,14-tetramethyl-2,6,10,14-nonadecatetraen-18-one (VI) in 20 ml of absolute ether was added in 25 minutes to sodium acetylide (prepared from 2.4 g of sodium and acetylene in 100 ml of liquid ammonia). The reaction mixture was stirred for 2 hours, and then allowed to stand for 15 hours at 20°. The workup was the same as described for the preparation of 2,6,10,14-tetramethyl-2,6,10,15-hexadecatetraen-14-ol (V). The yield of acetylenic alcohol (VII) was 10.1 g (61.8%).

B.p. 132-137° (0.25 mm), d_4^{20} 0.8820, $n^{20}D$ 1.4892, MR_D 116.6; calc. 115.3.

Found %: C 84.19, 84.49; H 11.78, 11.64. $C_{25}H_{40}O$. Calculated %: C 84.20; H 11.31.

2,6,10,14,18-Pentamethyl-2,6,10,14,19-eicosapentaen-18-ol (VIII). Ten grams of 2,6,10,14,18-pentamethyl-2,6,10,14-eicosatetraen-19-yn-18-ol (VII) in 30 ml of petroleum ether was hydrogenated at 20° in the presence of 1.5 g of palladium catalyst and 0.08 g of quinoline. Yield 9.1 g (90.4%).

B.p. 138-140° (0.32 mm), d_4^{20} 0.8748, $n^{20}D$ 1.4846, MR_D 117.4; calc. 116.84.

Found %: C 83.83; H 12.10. $C_{25}H_{42}O$. Calculated %: C 83.73; H 11.81.

IR-spectrum: 3400 (strong), 2900 (very strong), 1725 (medium), 1660 (weak), 1465 (very strong), 1390 (very strong), 1285 (weak), 1165 (weak), 1000 (weak), 910 (weak), 840 (weak), 760 (weak) cm^{-1}.

2,6,10,14,18-Pentamethyl-2,6,10,14,18-tricosapentaen-22-one (IX). (IX) was obtained by heating 12 g of 2,6,10,14,18-pentamethyl-2,6,10,14,19-eicosapentaen-18-ol (VIII) and 20 g of acetoacetic ester in a nitrogen stream at 175-180° for 55 hours. The yield of (IX) was 6 g (44.99%).

B.p. 134-138° (0.4 mm), d_4^{20} 0.8790, $n^{20}D$ 1.4838, MR_D 129.70; calc. 129.18.

Found %: C 84.15; H 11.40. $C_{25}H_{46}O$. Calculated %: C 84.35; H 11.63.

IR-spectrum: 3400 (weak), 2900 (very strong), 1730 (strong), 1615 (weak), 1465 (very strong), 1390 (medium), 1330 (weak), 1275 (weak), 1175 (weak), 1120 (weak), 1050 (weak), 980 (weak), 900 (weak), 835 (weak), 760 (weak), 710 (weak) cm^{-1}.

2,6,10,14,18,22-Hexamethyl-2,6,10,14,18-tetracosapentaen-23-yn-22-ol (X). Alcohol (X) was synthesized in the same manner as 2,6,10,14-tetramethyl-2,6,10-hexadecatrien-15-yn-14-ol (IV) and 2,6,10,14,18-pentamethyl-2,6,10,14-eicosatetraen-19-yn-18-ol (VII) from 10 g of 2,6,10,14,18-pentamethyl-2,6,10,14,18-tricosapentaen-22-one (IX), 1.4 g of sodium in 120 ml of liquid ammonia, and excess acetylene. The yield of (X) was 4 g (37.55%).

B.p. 137-140° (0.4 mm), d_4^{20} 0.8814, $n^{20}D$ 1.4850. MR_D 138.10; calc. 137.93.

Found %: C 84.99; H 11.36. $C_{30}H_{48}O$. Calculated %: C 84.84; H 11.40.

2,6,10,14,18,22-Hexamethyl-2,6,10,14,18,23-tetracosahexaen-22-ol (I). Four grams of 2,6,10,14,18,22-hexamethyl-2,6,10,14,18-tetracosapentaen-23-yn-22-ol (X) in 25 ml of petroleum ether was hydrogenated in the same manner as (IV) and (VII) at 22° in the presence of 1.4 g of palladium catalyst and 0.04 g of quinoline. Yield 3.5 g (87.5%).

B.p. 124-125° (0.3 mm), d_4^{20} 0.8696, $n^{20}D$ 1.4830, MR_D 140.20; calc. 139.46.

Found %: C 84.56, 84.60; H 11.59, 11.62. $C_{30}H_{50}O$. Calculated %: C 84.45; H 11.81.

IR-spectrum: 3400 (medium), 2900 (very strong), 1730 (weak), 1650 (weak), 1465 (very strong), 1390 (strong), 1330 (weak), 1280 (weak), 1170 (weak), 1120 (weak), 1000 (medium), 940 (weak), 905 (medium), 830 (medium), 760 (weak) cm^{-1}.

SUMMARY

1. The total synthesis of 2,6,10,14,18,22-hexamethyl-2,6,10,14,18,23-tetracosahexaen-22-ol (farnesylnerolidol) was accomplished.

2. In the course of the synthesis the following compounds were isolated and characterized: 2,6,10-trimethyl-2,6,10-pentadecatrien-14-one; 2,6,10,14-tetramethyl-2,6,10-hexadecatrien-15-yn-14-ol; 2,6,10-14-tetramethyl-2,6,10,15-hexadecatetraen-14-ol; 2,6,10,14-tetramethyl-2,6,10,14-nonadecatetraen-18-one; 2,6,10,14,18-pentamethyl-2,6,10,14-eicosatetraen-19-yn-18-ol; 2,6,10,14,18-pentamethyl-2,6,10,14,19-eicosapentaen-18-ol; 2,6,10,14,18-pentamethyl-2,6,10,14,18-tricosapentaen-22-one; 2,6,10,14,18,22-hexamethyl-2,6,10,14,18-tetracosapentaen-23-yn-22-ol.

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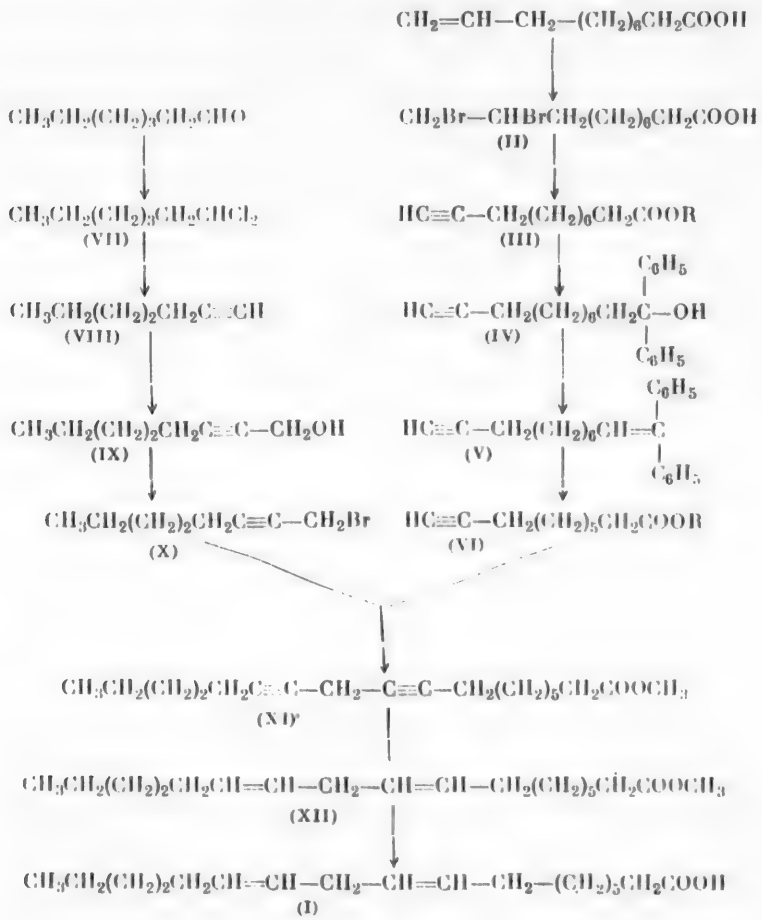
SYNTHESIS OF 9,12-OCTADECADIENOIC ACID

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Linoleic acid (I), as a complex with other natural-occurring unsaturated acids of the aliphatic series, namely linolenic and arachidonic acids, is known in medical practice as Vitamin F [1]. Together with other preparations, it is used in the treatment of certain ailments connected with interference in the exchange of materials [2], and it is also recommended as an agent for increasing the resistance of the organism to infectious diseases [3] and x-ray irradiation [4]. Triglycerides, containing linoleic acid radicals, are the main constituent of sunflower oil, and also of a number of other vegetable oils. The known methods for the synthesis of linoleic acid (I) are either based on the use of difficulty available raw materials, or include laborious steps [5].

We were able to synthesize 9,12-octadecadienoic acid (I) from 10-undecylenic acid (undecylenic acid) and 1-heptanal (enanthole), both being intermediate products in a number of chemical industries [6].



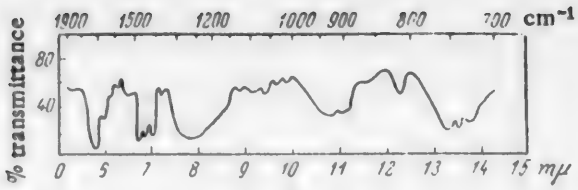


Fig. 1. Infrared spectrum of 9,12-octadecadienoic (linoleic) acid (I).

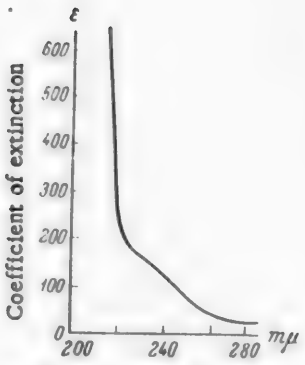


Fig. 2. Ultraviolet spectrum of 9,12-octadecadienoic (linoleic) acid (I).

The starting undecylenic acid was brominated to 10,11-dibromoundecanoic acid (II), which by subsequent dehydrobromination was converted to 10-undecynoic acid (III, R = H). This acid was then converted to the methyl ester (III, R = CH_3), and the latter reacted with phenylmagnesium bromide gave 1,1-diphenyl-10-undecynol (IV). Compound (IV) was dehydrated to 1,1-diphenyl-1-undecen-10-yne (V), and the latter by destructive oxidation was converted to 9-decynoic acid (VI, R = H). The methyl ester of this acid (VI, R = CH_3) was used as one of the intermediates in the synthesis of linoleic acid (I).

We used enanthole to obtain the second structural element in this synthesis, namely 1-bromo-2-octyne (X). For this enanthole was converted via 1,1-dichloroheptane (VII) to 1-heptyne (VIII), which as the organomagnesium compound was reacted with formaldehyde, and the thus obtained 2-octynol (IX) was reacted with phosphorus tribromide. Condensation of the magnesium bromide derivative of the methyl ester of 9-decynoic acid (VI) with 1-bromo-2-octyne (X) in the presence of cuprous chloride gave the methyl ester of 9,12-octadecadiynoic acid (XI). Selective hydrogenation of the methyl ester of 9,12-octadecadiynoic acid (XI), followed by subsequent saponification of (XII) led to linoleic acid (I). The structure of the thus synthesized acid (I) was confirmed by its physicochemical constants and the spectral analysis data [7] (see Figs. 1 and 2).

EXPERIMENTAL

10,11-Dibromoundecanoic Acid (II). To a solution of 23.01 g of undecylenic acid in 70 ml of chloroform, cooled to 0°, was added 20.19 g of bromine in 2 hours. After stirring for 2 hours at 18-20°, the solvent was distilled from the reaction mass, and the residue was fractionally distilled. Yield 33.31 g (77.5%). B.p. 192.4-194° (0.5 mm), b.p. 38.6-39.9° (from petroleum ether).

10-Undecynoic Acid (III, R = H). A mixture of 33.31 g of 10,11-dibromoundecanoic acid (II), 16.21 g of KOH and 150 ml of alcohol was heated in a 1000-ml autoclave for 1 hour at 145-150°. Here the pressure in the autoclave reached 10-12 atm. After cooling to 18-20°, the obtained precipitate was filtered and washed with 150 ml of alcohol. The solvent was distilled from the combined filtrates. The residue was treated with 50 ml of water, and then acidified at 0° with sulfuric acid. The reaction product was extracted with 100 ml of ether. The extract was dried over sodium sulfate. The residue after distilling off the solvent was distilled. Yield 14.06 g (79.7%).

B.p. 165.5-167° (3 mm), 155-159.6° (0.5 mm), m.p. 42.5-43.8°.

Found %: C 72.40, 72.71; H 10.10, 10.32. $C_{11}H_{18}O_2$. Calculated %: C 72.54; H 9.96.

Methyl Ester of 10-Undecynoic Acid (III, R = CH_3). A solution of 14.06 g of 10-undecynoic acid (III, R = H) in 93.5 ml of anhydrous methyl alcohol, previously saturated at 0° with dry HCl, was heated under reflux for 6 hours in a stream of dry HCl. Then the excess methyl alcohol was distilled off. The residue was cooled to 1-0° and neutralized with saturated aqueous sodium bicarbonate solution, followed by extraction of the reac-

Compound	Boiling point	Yield (in %)	d_4^{20}	$n^{20}D$	MR_D	
					found	calculated
2-Heptyne	111-113.4°	19.3	0.7504	1.4189	32.35	32.46
3-Heptyne	105.3-106.2	10.4	0.7492	1.4176	32.39	32.46

tion product with 200 ml of ether. The combined extracts were dried over sodium sulfate. The residue after distilling off the solvent was distilled. Yield 13.81 g (91.2%).

B.p. 109.5-111.5° (3 mm), d_4^{20} 0.9237, $n^{20}D$ 1.4501, MR_D 57.12; calc. 57.21.

Found %: C 73.30; H 10.41. $C_{12}H_{20}O_2F$. Calculated %: C 73.41; H 10.27.

1,1-Diphenyl-10-undecynol (IV). A solution of 13.81 g of methyl 10-undecynoate (III, R = CH_3) in 30 ml of absolute ether was added, with external cooling to -10°, in 45 minutes to the Grignard reagent, prepared from 5.98 g of magnesium turnings and 38.6 g of bromobenzene in 50 ml of absolute ether. The reaction mixture was heated under reflux for 2 hours, and then acidified at 0° with 80 ml of sulfuric acid (d_4^{20} 1.1). Here two layers were formed. The upper layer was separated. The product in the lower layer was extracted with 200 ml of ether. The combined extracts were neutralized with saturated aqueous sodium bicarbonate solution, and then dried over sodium sulfate. The residue after distilling off the solvent was distilled. Yield 16.81 g (74.6%). B.p. 142.5-144.8° (0.3 mm).

1,1-Diphenyl-1-undecen-10-yne (V). A solution of 16.81 g of 1,1-diphenyl-10-undecynol (IV) in 80 ml of dry toluene was heated under reflux for 6 hours in the presence of 0.05-0.07 g of iodine in a stream of nitrogen. The water formed during reaction was distilled off into a water separator. Then the reaction mass was cooled to 18-20°, and washed with 50 ml of 10% aqueous sodium thiosulfate solution. Then the product was dried over sodium sulfate. The solvent was distilled off and the residue was distilled. Yield 14.87 g (93.7%).

B.p. 169.5-173 (0.4 mm), d_4^{20} 1.1090, $n^{20}D$ 1.5620, MR_D 88.45; calc. 88.28.

Found %: C 91.65, 91.56; H 8.40, 8.41. $C_{23}H_{26}$ F. Calculated %: C 91.35; H 8.66.

9-Decynoic Acid (VI, R = H). To a mixture of 14.87 g of 1,1-diphenyl-1-undecen-10-yne (V) in 250 ml of glacial acetic acid at 55-66°, with mechanical stirring, in 2 hours, was added a solution of 10.35 g of chromic anhydride in 10 ml of water. After stirring for 8 hours at 80-95° the acetic acid was distilled from the reaction mass. The residue was treated with 240 ml of sulfuric acid (d_4^{20} 1.1), and the whole heated on the boiling water bath for 1 hour. Then 250 ml of saturated sodium chloride solution was added, and the separated material was extracted with 150 ml of ether. The combined extracts were neutralized with saturated aqueous sodium bicarbonate solution. The water layer was separated, acidified with sulfuric acid (d_4^{20} 1.10, to congo), and extracted with 180 ml of ether. The combined extracts were dried over sodium sulfate. The residue after distilling off the solvent was distilled. Yield 4.86 g (58.7%).

B.p. 109.2-112° (0.5 mm), 100-104.6° (0.2 mm), d_4^{20} 0.9993, $n^{20}D$ 1.4778, MR_D 47.63, $C_{10}H_{16}O_2F$. Calculated 47.85.

Methyl Ester of 9-Decynoic Acid (VI, R = CH_3). The reaction was run in the same manner as for the methyl ester of 10-undecynoic acid (III, R = CH_3), starting with 4.86 g of 9-decynoic acid (VI, R = H) and 27.8 g of methyl alcohol, previously saturated with HCl. Yield 4.71 g (89.3%).

B.p. 89-93.8° (0.5 mm), 126.5-128.5° (2 mm), d_4^{20} 1.047, $n^{20}D$ 1.5143, MR_D 52.44; calc. 52.58.

Found %: C 72.52, 72.77; H 9.81, 9.79. $C_{11}H_{18}O_2F$. Calculated %: C 72.54; H 9.96.

1,1-Dichloroheptane (VII). To 41.95 g of phosphorus pentachloride, cooled to 0°, with constant stirring, was added 22.87 g of enanthole in 2 hours. The reaction mass was allowed to stand at 18-20° for 4 hours, after which it was poured into 100 g of cracked ice, and the reaction product extracted with ether. The combined extracts were neutralized with saturated aqueous sodium bicarbonate solution, and then dried over calcium chloride. The residue after distilling off the solvent was distilled. Yield 23.32 g (68.9%).

B.p. 70.5-73.4° (10 mm), d_4^{20} 1.024, $n^{20}D$ 1.4478, MR_D 44.20. $C_7H_{14}Cl_2$. Calculated 44.26.

1-Heptyne (VIII). A mixture of 23.32 g of 1,1-dichloroheptane (VII) and 15.49 g of pulverized KOH was charged into a 300-ml iron cylindrical vessel, fitted with thermocouple (iron-constantan), Wurtz head, and descending condenser. The reaction mixture was heated to 200°, and the fraction with b.p. 90-99° (757 mm) was distilled off. The distillate was collected in a receiver, cooled to -7 to -10°. After drying over calcium chloride, the distillate was fractionally distilled through a column (having an efficiency of 35 theoretical plates). The yield of 1-heptyne (VIII) was 6.02 g (45.3%).

B.p. 97.3-98.9° (759 mm), d_4^{20} 0.7485, $n^{20}D$ 1.4179, MR_D 32.37. $C_7H_{12}F$. Calculated 32.46.

The constants and yields of the other 1-heptyne isomers, obtained in the above reaction, are summarized in the table.

2-Octynol (IX). With cooling to -5 to -8°, a solution of 6.02 g of 1-heptyne (VIII) in 50 ml of dry ether was added with vigorous stirring to the Grignard reagent, prepared from 3.06 g of magnesium turnings, 13.71 g of ethyl bromide and 50 ml of absolute ether. The reaction mass was heated under reflux for 2 hours. Then formaldehyde, obtained from the depolymerization of 11.34 g of dry paraform, was passed into the reaction mass for 4 hours at 0 to -5°. The reaction product of the Grignard reagent with formaldehyde was decomposed with water at -5 to -10°. The water layer was separated and the product was extracted from it with 150 ml of ether. The combined extracts were dried over sodium sulfate, then the solvent was distilled off, and the residue was fractionally distilled. Yield 4.68 g (59.4%).

B.p. 100.3-104.5° (18 mm), d_4^{20} 0.8923, $n^{20}D$ 1.4555, MR_D 38.41. $C_8H_{14}OF$. Calculated 38.61.

1-Bromo-2-octyne (X). To a solution of 4.68 g of 2-octynol (IX) in 30 ml of absolute ether at 0° was added 10.08 g of phosphorus tribromide in 30 minutes. The reaction mass was heated under reflux for 2 hours, then with cooling to -5 to -10° it was decomposed with 50 ml of ice water, and finally it was neutralized with saturated aqueous sodium bicarbonate solution. The water layer was extracted with 100 ml of ether, and the combined extracts were dried over sodium sulfate. The residue after distilling off the solvent was distilled. Yield 3.34 g (47.5%).

B.p. 69-71.9° (4.5 mm), d_4^{20} 1.2100, $n^{20}D$ 1.4863, MR_D 44.89. $C_8H_{13}BrF$. Calculated 44.84.

Methyl Ester of 9,12-Octadecadiynoic Acid (XI). A solution of 4.71 g of methyl 9-decynoate (VI, R = CH_3) in 20 ml of absolute ether was added at 0 to -2°, in 25 minutes, to the Grignard reagent, prepared from 0.430 g of magnesium turnings and 1.93 g of ethyl bromide in 40 ml of absolute ether. The reaction mass was heated under reflux for 1 hour, after which 0.25 g of dry cuprous chloride was added, the whole refluxed for 15 minutes, and then 3.34 g of 1-bromo-2-octyne (X) in 50 ml of absolute ether was added gradually. Then the mixture was refluxed for 2 hours, 60 ml of dry toluene was added, and having distilled off the ether, the reaction mass was heated under reflux for 15 hours in a stream of nitrogen, after which it was treated with 50 ml of ice water, and then acidified with sulfuric acid (d_4^{20} 1.10). The ether layer was separated. The product in the water layer was extracted with 150 ml of ether. The combined extracts were dried over sodium sulfate. The residue after distilling off the solvent was distilled. Yield 0.751 g (14.7%).

B.p. 159-161° (0.5 mm), m.p. 12.8-13.3°, d_4^{25} 0.9620, $n^{25}D$ 1.4899, MR_D 87.28; calc. 87.47.

Found %: C 78.75, 78.56; H 10.78, 10.49. $C_{19}H_{30}O_2F$. Calculated %: C 78.56; H 10.41.

Methyl Ester of 9,12-Octadecadienoic (Linoleic) Acid (XII). With mechanical agitation, a solution of 0.751 g of methyl 9,12-octadecadiynoate (XI) in 15 ml (1 : 3) of anhydrous alcohol and dry benzene was hydrogenated at 18-20° in the presence of 0.14 g of palladium catalyst for 6 hours (130.5 ml of H_2 was absorbed, theoret. calculation for two triple bonds is 131.9 ml of H_2). The catalyst was filtered and washed with 20 ml of benzene. The solvent was distilled from the combined extracts, and the residue was distilled. Yield 0.639 g (83.6%).

B.p. 169-171.5° (0.9 mm), d_4^{20} 0.9012, $n^{20}D$ 1.4675; MR_D 90.74; calc. 90.66.

Found %: C 77.21, 77.20; H 11.82, 11.61. $C_{19}H_{34}O_2F_2$. Calculated %: C 77.52; H 11.63.

9,12-Octadecadienoic Acid (I). A solution of 0.122 g of KOH in 30 ml of methyl alcohol was added to a solution of 0.639 g of methyl 9,12-octadecadienoate (XII). The reaction mass was kept for 12 hours at 18-20° in

a stream of nitrogen, and then the methyl alcohol was distilled off. The precipitate was dissolved in 20 ml of water, and the unsaponified material was extracted with 70 ml of ether. The water layer was acidified with sulfuric acid (d_4^{20} 1.10, to congo), and the product extracted with 100 ml of ether. The obtained extract was dried over sodium sulfate. The residue after distilling off the solvent was distilled. Yield 0.49 g (80.5%).

B.p. 160-164° (0.5 mm), d_4^{20} 0.9118, $n^{20}D$ 1.4718, MR_D 86.12; calc. 85.93.

Found %: C 76.95, 77.46; H 11.40, 11.57. $C_{18}H_{32}O_2F_2$. Calculated %: C 77.11; H 11.50.

Tetrabromide, $C_{18}H_{32}O_2Br_4$, m.p. 113-114° (from petroleum ether).

SUMMARY

The synthesis of 9,12-octadecadienoic acid was accomplished.

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SYNTHESIS OF 1-ACYL-2-CHLORO-1-CYCLOPENTENES AND ETHYLENE KETALS OF 2-ACYLCYCLOPENTANONES

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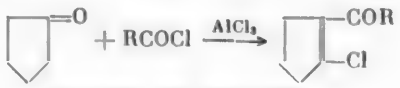
Moscow State University

The wide use of β-chlorovinyl ketones and their close derivatives in synthesis work raises the need of developing methods for the synthesis of new types of compounds, belonging to this class.

Syntheses of β-chlorovinyl ketones with an open chain, namely alkyl [1, 2], alkenyl [3] and aryl β-chlorovinyl ketones [4, 5], have been worked out in detail at the present time. However, compounds of this type, belonging to the alicyclic series, are practically unknown. Two brief communications, contradicting each other, exist in the literature on the possibility of synthesizing 1-acyl-2-chlorocyclohexenes by the condensation of cyclohexanone with acetyl chloride under the influence of aluminum chloride [6, 7]. Recently this reaction was studied in detail by us [8], in which connection we were able to show that it leads mainly to 1-acyl-2-chloro-2-cyclohexene, while the more interesting reaction product, namely 1-acyl-2-chloro-1-cyclohexene is formed only in small amount. In the same paper we also stated that in contrast to this, cyclopentanone when reacted with acetyl chloride in the presence of aluminum chloride yields 1-acetyl-2-chloro-1-cyclopentene, a cyclic analog of β-chlorovinyl ketones.

In view of the fact that this reaction still remains as the solitary route to new compounds of the indicated type, we decided to make a more detailed study of it.

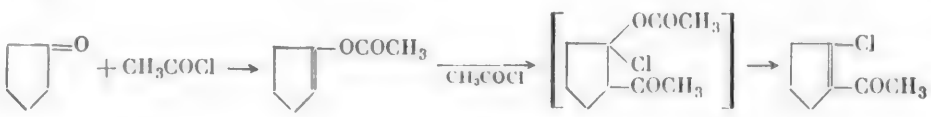
The reaction of cyclopentanone with acid halides in the presence of aluminum chloride has a fairly general character and leads to the formation of new 1-acyl-2-chloro-1-cyclopentenes in 30-40% yields.



R = CH_3, C_2H_5, C_3H_7, C_4H_9.

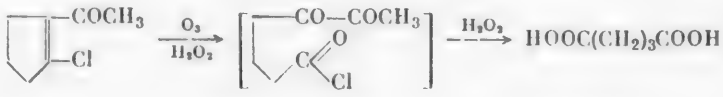
An attempt to react benzoyl chloride in the indicated sense has so far been unsuccessful, and instead of the desired β-chloro ketone we obtained a crystalline substance with m.p. 20°, devoid of chlorine, the structure of which has not yet been established.

The best results in the investigated reaction are obtained if the acid chloride and aluminum chloride are prepared as a complex in dichloroethane, to which the cyclopentanone is then added. The use of other solvents, for example carbon disulfide, gives poorer results. The reaction time requires several hours, and should be increased in going from acetyl chloride to its higher homologs. As regards the mechanism of this reaction, then as we had already indicated in the case of cyclohexanone [8], it apparently goes through the formation of the corresponding enol ester.



In the present case this is also confirmed by the fact that we were able to obtain 1-acetyl-2-chloro-1-cyclopentene, to be sure, in much lower yield, by the reaction of the enol acetate of cyclopentanone with acetyl chloride in the presence of aluminum chloride.

All of the 1-acyl-2-chloro-1-cyclopentenes obtained by us were colorless oily liquids, quite unstable when stored, in which respect they greatly resemble the alkyl β-chlorovinyl ketones. As was indicated in a previous paper [8], the position of the double bond in them, conjugated with the carbonyl group, is shown on the example of the first member of the series by the nature of the absorption maximum of its 2,4-dinitrophenylhydrazone. We obtained conclusive proof as to their structure by the ozonolysis of 1-acetyl-2-chloro-1-cyclopentene. Decomposition of the ozonide in the presence of hydrogen peroxide gave as the solitary reaction product only glutaric acid, identified as the bis-p-bromophenylacyl ester.



It is natural that if the obtained compound was the isomeric 1-acetyl-2-chloro-2-cyclopentene (or contained this isomer as impurity), then the ozonolysis product would prove to be the β-ketodicarboxylic acid, which after ketonic decomposition, occurring under the conditions for the decomposition of ozonides of such type, would give, in the final analysis, δ-ketocaproic acid.

Consequently, it can be assumed to have been conclusively established that whereas in the cyclohexanone series the main reaction product of the ketone with acid chloride is the β,γ-unsaturated ketone, in the cyclopentanone series the reaction goes in a well-defined manner and gives the α,β-unsaturated ketone, a cyclic analog of β-chlorovinyl ketones. This difference in the behavior of five- and six-membered rings we are inclined to explain as being due to a difference in the elimination of the elements of acetic acid from the addition product, which appears as a consequence of the difference in the conformation of the two cyclic systems.

A study of the reactions of the obtained compounds for the purpose of comparing them with β-chlorovinyl ketones was of great interest, in particular, elucidating the mobility of the halogen atom in them, this being the most characteristic trait of the chemical behavior of β-chlorovinyl ketones [9]. Study revealed that although the obtained compounds have a more labile chlorine than is present in vinyl chloride, still they are far inferior to the β-chlorovinyl ketones in this respect. Thus, for example, when 1-acetyl-2-chloro-1-cyclopentene is reacted with triethylamine the quaternary salt is formed only with heating and a long reaction time, as a result of which we were unable to isolate the salt in analytically pure form due to profound tarring of the reaction mixture; at the same time β-chlorovinyl ketones react with triethylamine with unusual vigor [10]. When 1-butyroyl-2-chloro-1-cyclopentene is reacted with sodium iodide under the conditions used for the corresponding reaction with β-chlorovinyl ketones [11], the reaction does not go, and the starting product is recovered completely on distillation. If the reaction is run under more drastic conditions, then tarring takes place. The reaction of 1-butyroyl-2-chloro-1-cyclopentene with p-nitrophenylhydrazine leads to the formation of the p-nitrophenylhydrazone, which we were unable to cyclize to the pyrazole derivative, whereas in the case of β-chlorovinyl ketones their phenylhydrazones show spontaneous cyclization [1, 12]. Several facts are responsible for such a low activity of the halide atom in 1-acyl-2-chlorocyclopentenes.

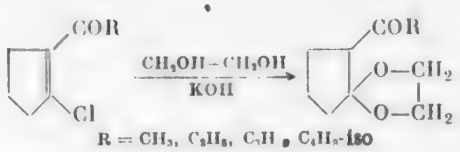
1. The obtained compounds show a cis-configuration as regards the mutual position of the acyl group and chlorine atom, whereas the β-chlorovinyl ketones have a trans-configuration [13]. Together with this, a transfer of the influence exerted by the carbonyl group on the halide atom should, naturally, be more effective for trans-compounds.

2. Together with the halide, the obtained compounds have a substituent in the β-position. It is known [14] that β-chlorovinyl ketones of this type are characterized by a much less labile halide atom.

3. In the case of replacing the halide atom by a bimolecular mechanism the attacking nucleophilic reagent should approach from the side opposite the chlorine atom, which is impossible in the given case due to the presence of a planar ring.

It is probable that all three factors play some part here; the problem of which plays the determining role is being investigated by us at the present time.

Despite the quite low activity of the halogen atom in 1-acyl-2-chloro-1-cyclopentenes, still we were able to utilize the latter to prepare some previously unknown ketals of 2-acylcyclopentanones, being analogs of β-keto aldehydes, which, in the synthetic sense, are the most important derivatives of β-chlorovinyl ketones [11, 15]. The reaction of 1-acyl-2-chloro-1-cyclopentenes with alcohol is ill-defined and gives a mixture of substances, from which it is difficult to isolate individual compounds. On the other hand, reaction with ethylene glycol in the presence of KOH, similar to the case of reaction with β-chlorovinyl ketones [16], gives cyclic ketals.



R = CH_3, C_2H_5, C_3H_7, C_4H_9-iso

In the present case reaction is much slower than in the case of β-chlorovinyl ketones, and requires several days for its completion. Heating is required to obtain the higher ketals. The yields of β-keto ketals are quite high and reach 50-75%.

The indicated reaction is of interest for the reason that only recently are the β-keto acetals beginning to find constantly broader synthetic use.

EXPERIMENTAL

1-Acetyl-2-chloro-1-cyclopentene. To 134 g of aluminum chloride in 250 ml of dry dichloroethane, with ice cooling and vigorous stirring, was added 78.5 g of acetyl chloride, and after all of the aluminum chloride had dissolved, 42 g of cyclopentanone was added slowly. After stirring for 2 hours at room temperature, the reaction mass was poured into a mixture of ice and hydrochloric acid, after which the lower layer was separated, and the water layer was extracted twice with dichloroethane. The combined dichloroethane solution was dried over calcium chloride, and the dichloroethane was distilled off under a slight vacuum. Fractional distillation of the oily residue gave 21.7 g of cyclopentanone with b.p. 38-40° (25 mm), and 10.6 g (31%), based on reacted cyclopentanone) of 1-acetyl-2-chloro-1-cyclopentene with b.p. 90-92° (22 mm). After redistillation the substance had the following constants:

B.p. 91-92° (22 mm), $n^{20}D$ 1.5045, d_4^{20} 1.1429, MR_D 37.45; calc. 36.74.

Found %: C 58.18, 58.35; H 6.50, 6.35. C_7H_9OCl. Calculated %: C 58.20; H 6.28.

The compound is a colorless oil, miscible with the ordinary organic solvents. It is extremely unstable when stored.

The 2,4-dinitrophenyl hydrazone, obtained in known manner [17], appeared as bright red crystals with m.p. 174-175° (from glacial acetic acid).

Found %: N 17.47, 17.29. $C_{13}H_{13}O_4N_4Cl$. Calculated %: N 17.31.

When the reaction was run under similar conditions in carbon disulfide solution the yield of 1-acetyl-2-chloro-1-cyclopentene was 22%, based on reacted cyclopentanone.

1-Propionyl-2-chloro-1-cyclopentene. The compound was obtained in the same manner as the preceding from 28 g of cyclopentanone, 61 g of propionyl chloride and 89 g of aluminum chloride in 165 ml of dichloroethane, after stirring for 7.5 hours. Yield 10.1 g (37%, based on reacted cyclopentanone). Redistillation gave

B.p. 97-98° (13 mm), $n^{20}D$ 1.4952, d_4^{20} 1.1000, MR_D 42.09; calc. 41.35.

Found %: C 60.56, 60.72; H 7.02, 7.14. $C_8H_{11}OCl$. Calculated %: C 60.59; H 7.09.

The 2,4-dinitrophenylhydrazone was obtained as red crystals with m.p. 156-158° (from glacial acetic acid).

Found %: N 16.24, 16.16. $C_{14}H_{15}O_4N_4Cl$. Calculated %: N 16.58.

1-Butyroyl-2-chloro-1-cyclopentene. Obtained in the same manner as the preceding from 35 g of cyclopentanone, 87 g of butyroyl chloride and 110 g of aluminum chloride in 210 ml of dichloroethane, with stirring for 18 hours. Yield 18.9 g (38.2%), based on reacted cyclopentanone).

B.p. 106-107° (8 mm), $n^{20}D$ 1.4900, d_4^{20} 1.0746, MR_D 46.41; calc. 46.17.

Found %: C 62.47, 62.64; H 7.57, 7.72. $C_9H_{13}OCl$. Calculated %: C 62.63; H 7.79.

The 2,4-dinitrophenylhydrazone was obtained as red needles with m.p. 138-139° (from glacial acetic acid).

Found %: N 15.77, 15.70. $C_{15}H_{17}O_4N_4Cl$. Calculated %: N 15.98.

1-Isovaleroyl-2-chloro-1-cyclopentene. Obtained in a similar manner as before from 42 g of cyclopentanone, 120 g of isovaleroyl chloride and 134 g of aluminum chloride in 300 ml of dichloroethane, with stirring for 8 hours. Yield 22 g (36%, based on reacted cyclopentanone).

B.p. 74-75° (2 mm), $n^{20}D$ 1.4835, d_4^{20} 1.0360, MR_D 51.48; calc. 50.59.

Found %: C 64.59, 64.61; H 8.27, 8.31. $C_{12}H_{15}OCl$. Calculated %: C 64.33; H 8.20.

Reaction of Cyclopentanone With Benzoyl Chloride. Proceeding as before, we took for reaction 42 g of cyclopentanone, 70 g of benzoyl chloride and 134 g of aluminum chloride in 250 ml of dichloroethane. The reaction mixture was worked up in the usual manner to give 17 g of cyclopentanone, 40 g of benzoyl chloride and 12 g of a substance with b.p. 159-171° (3 mm). On redistillation the latter distilled at 149-150° (1 mm), and had $n^{20}D$ 1.4815, and m.p. 20-21°.

This substance was found to be free of chlorine. White crystals, soluble in all organic solvents. The substance is stable to storage.

Reaction of Cyclopentanone Enol Acetate With Acetyl Chloride. When 20.5 g of the enol acetate, obtained by the reaction of cyclopentanone with isopropenyl acetate in known manner [18], was heated with 13.6 g of acetyl chloride and 21.5 g of aluminum chloride in 80 ml of dichloroethane for 7 hours with stirring, and the reaction mixture worked up as described before, we obtained 2.4 g (10.4%) of 1-acetyl-2-chloro-1-cyclopentene.

B.p. 93-94° (23 mm), $n^{20}D$ 1.5039, d_4^{20} 1.1420.

The 2,4-dinitrophenylhydrazone had m.p. 173-174.5°. Its m.p. was not depressed when mixed with the 2,4-dinitrophenylhydrazone of the product obtained in Expt. 1.

Ozonolysis of 1-Acetyl-2-chloro-1-cyclopentene. With ice cooling, a stream of ozonized oxygen (~2% ozone) was passed into a solution of 1.7 g of 1-acetyl-2-chloro-1-cyclopentene in 12 ml of dry chloroform for 6 hours at a rate of 6.5 liters per hour. Then 25 ml of water and 3 ml of perhydrol were added to the solution, and the whole stirred for 3 hours at 45-50°, after which it was extracted with aqueous sodium carbonate solution. The alkaline extract was washed with ether, acidified (to congo), and again extracted with ether. Removal of the solvent by evaporation left an oil, which crystallized on standing for several hours. The obtained glutaric acid was identified by converting it in conventional manner [19] to the bis-p-bromophenylacyl ester with m.p. 137.5-138° (from alcohol). The mixed melting point with an authentic specimen was not depressed.

Reaction of 1-Butyroyl-2-chloro-1-cyclopentene With p-Nitrophenyl-hydrazine. To a solution of 1.76 g of p-nitrophenylhydrazine in 30 ml of glacial acetic acid was added 2 g of 1-butyroyl-2-chloro-1-cyclopentene. Yellow needle crystals began to deposit almost immediately. The next day they were suction-filtered and washed on the filter with absolute ether. Yield 3.5 g (quantitative). M.p. 140.5° (from alcohol).

Found %: N 14.03, 14.21. $C_{15}H_{18}O_2N_3Cl$. Calculated %: N 13.79.

The substance remained unchanged when heated to the melting point. Tarring occurred at a higher temperature.

Reaction of 1-Butyroyl-2-chloro-1-cyclopentene With Sodium Iodide. Six grams of 1-butyroyl-2-chloro-1-cyclopentene was added to a solution of 6.1 g of sodium iodide in 20 ml of acetone. The mixture was allowed to stand at room temperature for several hours and then heated on the water bath for 4 hours, after which it was poured into water. The oil was extracted with ether, dried over sodium sulfate, the ether evaporated, and 5 g of unchanged 1-butyroyl-2-chloro-1-cyclopentene, with b.p. 81-84° (4 mm) and $n^{20}D$ 1.4927, was isolated from the residue.

Running the reaction for a longer time (20 hours) led to complete tarring of the reaction mixture.

2-Acetylcyclopentanone Ethylene Ketal. With ice-water cooling and stirring, 8.9 g of 1-acetyl-2-chloro-1-cyclopentene was added to a solution of 3.5 g of KOH in 11.5 ml of ethylene glycol. After stirring for 70 hours

the mixture was poured into water and extracted with ether, after which the ether extracts were dried over calcium chloride and the ether distilled off. Fractional distillation of the residue gave 5.2 g(50%) of substance.

B.p. 115-116° (16 mm), $n^{20}D$ 1.4700, d_4^{20} 1.1170, MR_D 42.50; calc. 42.67.

Found %: C 63.79, 63.67; H 8.50, 8.45. $C_9H_{14}O_3$. Calculated %: C 63.52; H 8.29.

The colorless oil is miscible with organic solvents. It is relatively stable to storage. It gives an intense color with ferric chloride.

2-Propionylcyclopentanone Ethylene Ketal. A mixture of 4.15 g of 1-propionyl-2-chloro-1-cyclopentene with a solution of 1.7 g of KOH in 9 ml of glycol was stirred for 48 hours at room temperature, then for 10 hours at 50-60°, and after this it was poured into water and worked up as indicated above. Yield 3.55 g (74%).

B.p. 118-121° (12 mm), $n^{20}D$ 1.4703, d_4^{20} 1.0905, MR_D 47.18; calc. 47.03.

Found %: C 65.60, 65.67; H 8.97, 9.03. $C_{10}H_{16}O_3$. Calculated %: C 65.40; H 8.70.

2-Butyroylcyclopentanone Ethylene Ketal. A mixture of 5.2 g of 1-butyroyl-2-chloro-1-cyclopentene with a solution of 1.9 g of KOH in 10 ml of glycol was stirred for 10 hours at room temperature, 10 hours at 40-45°, and 10 hours at 50-55°, after which it was worked up in the usual manner. Yield 3.8 g (63.5%).

B.p. 105.5-107° (5 mm), $n^{20}D$ 1.4713, d_4^{20} 1.0711, MR_D 51.77; calc. 51.92.

Found %: C 66.52, 66.74; H 9.03, 9.00. $C_{11}H_{18}O_3$. Calculated %: C 66.62; H 9.08.

2-Isovaleroylcyclopentanone Ethylene Ketal. A mixture of 5.3 g of 1-isovaleroyl-2-chloro-1-cyclopentene and a solution of 1.8 g of KOH in 10 ml of glycol was stirred for 10 hours at room temperature, 10 hours at 40-45°, 10 hours at 50-55°, and 8 hours at 60-65°, after which it was worked up in the usual manner. Yield 4 g (66%).

B.p. 101-102° (3 mm), $n^{20}D$ 1.4652, d_4^{20} 1.0350, MR_D 56.75; calc. 56.51.

Found %: C 68.10, 67.88; H 9.61, 9.61. $C_{12}H_{20}O_3$. Calculated %: C 68.00; H 9.47.

SUMMARY

1. 1-Acyl-2-chloro-1-cyclopentenes, cyclic analogs of β-chlorovinyl ketones, were obtained for the first time by the reaction of cyclopentanone with acid chlorides in the presence of aluminum chloride.

2. It was postulated that the indicated reaction goes through the formation of the enol acetate of cyclopentanone, which then reacts further on the type of the Kondakova-Krapivina reaction. This postulation was confirmed by preparing 1-acetyl-2-chloro-1-cyclopentene from cyclopentanone enol acetate and acetyl chloride under analogous conditions.

3. It was shown that the halide atom in 1-acyl-2-chloro-1-cyclopentenes is less labile than in β-chlorovinyl ketones, and some opinions were expressed as to the reasons for this lowered activity.

4. New ethylene ketals of 2-acylcyclopentanones were obtained by reacting 1-acyl-2-chloro-1-cyclopentenes with ethylene glycol in the presence of potassium hydroxide.

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BROMINATION OF β-KETO ACETALS

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Quite recently β-keto acetals, $RCOCH_2CH(OR')_2$, readily prepared from β-chlorovinyl ketones [1-3], are finding constantly broader use in synthetic organic chemistry. Up to now they were used either as potential β-dicarbonyl compounds [1, 4], to a certain degree duplicating the β-chlorovinyl ketones in their transformations, or as ketones, containing an additional reactive substituent [2, 3, 5-7]. Together with this, a third possibility remained completely unused, namely the introduction of substituents in the central methylene linkage of keto acetals for the purpose of utilizing the compounds obtained in this manner in highly varied syntheses. The only exception to this is a short statement by Plieninger that it is possible to oxidize β-keto acetals with lead tetraacetate [8].

A study of the problem of replacing the hydrogen atoms in the methylene group of β-keto acetals by other substituents also possesses independent interest, since this permits making some estimate of the influence exerted by the acetal group on the linkage adjacent to it, a problem that has remained quite obscure up to now.

We selected the bromination of keto acetals, a reaction not studied previously, as being the first reaction of this type. We used different bromination agents (N-bromosuccinimide, dioxane dibromide, bromine) in various solvents. The best results were obtained when the bromination was run with bromine in the presence of agents that tie up the hydrogen bromide; under these conditions the reaction goes quite well, in which connection the end result depends on the solvent used. Replacement of one of the hydrgen atoms in the central methylene linkage is observed when β-keto acetals are brominated with bromine in aqueous medium in the presence of barium carbonate; at the same time there occurs hydrolytic cleavage of the acetal group, with the end result that an α-bromo-β-keto aldehyde (α-bromohydroxymethylene ketone) is formed.

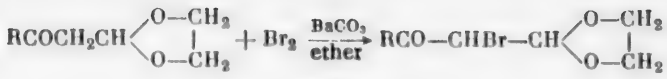
$$R{-}COCH_2CH\begin{matrix}OR'\\OR'\end{matrix} + Br_2 \xrightarrow[H_2O]{BaCO_3} RCOCHBrC\begin{matrix}O\\H\end{matrix}$$

$R = CH_3$, C_2H_5, C_3H_7, C_4H_9-iso
$R' = CH_3$, $R'{-}R' = CH_2{-}CH_2$.

Hydrolysis of the acetal group occurs independently of whether a dialkyl acetal or the more stable ethylene acetal is taken for reaction [3]. The obtained bromoketo aldehydes are crystalline compounds, rapidly darkening when stored. Some of the compounds belonging to this type were obtained by the bromination of the sodium derivatives of hydroxymethylene ketones [9, 10], but, as a rule, they were not isolated in a pure crystalline form. As is well known, this is due to the fact that hydroxymethylene ketones, serving as the starting materials, are themselves quite impure due to the ill-defined nature of the formylation reaction [11].

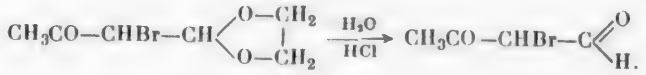
The method proposed by us for the preparation of α-bromo-β-keto acetals is free of this limitation, since in our case there is no doubt as to the purity of the starting β-keto acetal, and the reaction itself goes smoother than is the case with the bromination of hydroxymethylene ketones, leading to a 40-65% yield of bromoketo aldehydes.

Hydrolysis of the acetal grouping is avoided when the bromination of cyclic ethylene acetals of β-keto aldehydes [3] with bromine is run in absolute ether in the presence of dry barium carbonate, and the end result here is the ethylene acetal of the α-bromoketo aldehyde:



R = CH_3, C_2H_5, C_3H_7, C_6H_5.

The reaction goes smoothly, and the yields range from 40 to 60%. The new acetals of α-bromo-β-keto aldehydes are oily colorless substances with a sharp odor, turning dark with comparative rapidity when stored. The obtained acetals are easily hydrolyzed with dilute hydrochloric acid, as a result of which α-bromo-β-keto aldehydes are obtained, identical with the product obtained by bromination in aqueous medium, for example.



The conditions under which β-keto acetals are brominated indicate that essentially the mobility of the hydrogen atoms in their methylene linkage differs but slightly from the mobility of the α-methylene hydrogens in ketones, and in any case, is strongly different from the mobility of the corresponding atoms in β-dicarbonyl compounds. From this it is possible to conclude that the acetal grouping is essentially without influence on the methylene linkage adjacent to it. Nevertheless, we were unable to isolate any products of bromination at the other α-position, found in series with the carbonyl group. This indicates that the central methylene linkage in β-keto acetals contains hydrogen atoms that are considerably more active than are the analogous α-methylene hydrogens in the ketone. A similar conclusion was reached by Plieninger, who studied the oxidation of β-keto acetals with lead tetraacetate, and found that oxidation occurred only at the central methylene linkage [8].

The compounds obtained in the bromination of α-bromo-β-keto aldehydes and their acetals, being α-bromocarbonyl compounds, can be used extensively in various syntheses. Here we will mention only the synthesis of certain heterocyclic compounds. The heating of α-bromo-β-keto aldehydes with urea in acetone solution smoothly gives 2-amino-5-acyloxazoles in 50-60% yield:



R = CH_3, C_2H_5.

One example of such a reaction for the case of α-bromobezoylacetaldehyde was described earlier by Fodor [12]. Our results indicate that this reaction is also applicable to the aliphatic series, and since the bromination method developed by us makes the starting bromides readily available, this method of synthesizing 2-amino-5-acyloxazoles assumes preparative importance.

2-Amino-5-acylthiazoles are formed in high yield when α-bromo-β-keto aldehydes are reacted with thiourea; the corresponding acylthiazoles are formed less smoothly when condensation is with thioamides:



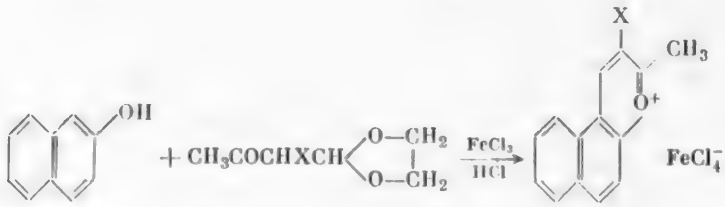
R = CH_3, C_2H_5
R = CH_3, R' = H, C_6H_5

In the indicated condensations the starting bromocarbonyl derivatives react not as α-bromo ketones, but as α-bromo aldehydes, since aldehydes are not formed, but instead ketones of the thiazole and oxazole series. This was shown by us in that the obtained compounds gave negative reactions for the aldehyde group, and also by the oxidation of 5-acetylthiazole (obtained by the condensation of α-bromo-β-keto-butyraldehyde with thioformamide) with potassium permanganate, where the known 5-thiazolecarboxylic acid was obtained.



This also at the same time indicates the structure of the initial α-bromo-β-ketoaldehyde. In fact, if bromination of the original β-ketoaldehyde proceeded along the methylene linkage, and not at the methyl group, then such a bromide, after condensation with thioformamide and subsequent oxidation, would not give 5-thiazolecarboxylic acid.

The obtained α-bromo-β-keto aldehydes and their acetals can also function as β-dicarbonyl compounds. This was demonstrated by us on the example of synthesizing naphthopyrylium salts, containing bromine in the pyrylium ring. Since the synthesis of naphthopyrylium salts from β-keto acetals had not been described before, we first ran the indicated reaction on the example of condensing the acetal of β-ketobutyraldehyde with β-naphthol in the presence of ferric chloride in a mixture of acetic and hydrochloric acids. Here we obtained 2-methylnaphtho [1, 2: 5', 6'] pyrylium chloroferrate, similar to the compound obtained earlier in our laboratory from methyl β-chlorovinyl ketone [13]. Under the same conditions, the acetal of α-bromo-β-ketobutyraldehyde gave 2-methyl-3-bromonaphtho [1, 2: 5', 6'] pyrylium chloroferrate, the first member of the previously unknown bromopyrylium salts.



This reaction shows that the keto acetals obtained by us can be used to synthesize bromine-containing heterocyclic compounds by the direct condensation of the indicated acetals with appropriate reagents.

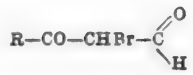
EXPERIMENTAL

Bromination of β-Keto Acetals in Aqueous Medium. With stirring and illumination of the reaction mixture with a strong electric lamp, 5.4 ml of bromine was added in drops to a mixture of 0.1 mole of the β-keto acetal, 10 g of barium carbonate and 25-30 ml of water. Several minutes after starting the reaction, the flask was heated cautiously on the water bath until vigorous reaction set in. When half of the bromine had been added the temperature of the mixture was up to 40-50°, and the heating was terminated. After all of the bromine had been added the mixture was stirred until it became colorless, then it was cooled, the lower layer separated, the upper layer extracted 3 times with ether, the extracts added to the main product, the whole dried over sodium sulfate, the ether evaporated under a slight vacuum, the crystalline residue filtered on a porous filter, washed with several ml of petroleum ether, then with 1-2 ml of chloroform, again with petroleum ether, and finally it was dried in a vacuum desiccator. The properties of the α-bromo-β-keto aldehydes obtained in this manner are summarized in Table 1.

Bromination of β-Keto Acetals in Ether. To a mixture of 0.1 mole of β-ketoaldehyde ethylene acetal and 20 g of barium carbonate in 35-45 ml of absolute ether (in the case of benzoylacetaldehyde, in 190-200 ml) was added, with stirring and illumination of the reaction mixture with a strong electric lamp, 5.3 ml of bromine in drops. The bromination went very slowly at first, and then it became vigorous. After all of the bromine had been added and the reaction mixture had decolorized, the latter was stirred for several minutes more, and the precipitate was filtered and washed thoroughly with absolute ether. The filtrate was dried over sodium sulfate, the ether was evaporated in vacuo, and the residue was distilled twice. In the case of the bromination of benzoylacetaldehyde the residue, after distilling off the ether, was placed in the refrigerator for several days, where it crystallized, after which it was filtered on a porous filter, and then recrystallized from methanol. The properties of the α-bromo-β-ketoaldehyde ethylene acetals obtained in such manner are summarized in Table 2.

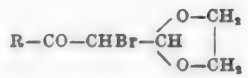
Hydrolysis of α-Bromo-β-ketobutyraldehyde Ethylene Acetal. A mixture of 1.5 g of the bromo acetal and 10 ml of 1N hydrochloric acid was stirred at room temperature for 40-50 minutes, after which the oil layer was

TABLE 1

Synthesis of α-Bromo-β-keto Aldehydes 

Expt. No.	R	Yield (in %)	Melting point	% C		% H		Remarks
				found	calculated	found	calculated	
1	CH_3	40	108.5—109.5°	28.61, 29.05	28.66	3.17, 3.15	3.14	The ethylene acetal was brominated
2	CH_3	51	109—110	—	—	—	—	The dimethyl acetal was brominated
3	C_2H_5	50.5	90—91	33.90, 33.70	33.74	4.08, 3.98	4.00	The same
4	C_3H_7	65	68—68.5	37.36, 37.42	37.43	4.57, 4.70	4.77	" "

TABLE 2

Synthesis of α-Bromo-β-ketoaldehyde Ethylene Acetals 

Expt. No.	R	Yield (in %)	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	MR_D		% C		% H	
						found	calculated	found	calculated	found	calculated
1	CH_3	41	104—104.5°(6)	1.4938	1.5840	38.50	38.77	34.19, 34.41	34.14	4.29, 4.30	4.31
2	C_2H_5	42.6	100—101 (3)	1.4892	1.4907	43.30	43.38	38.07, 37.91	37.67	4.47, 4.82	4.90
3	C_3H_7	53.5	99—100 (1)	1.4852	1.4319	47.70	48.01	40.64, 40.66	40.48	5.67, 5.48	5.69
4	C_6H_5	58	M.p. 68.5—69	—	—	—	—	48.77, 48.71	48.77	4.20, 4.06	4.22

separated, while the water layer was extracted 3 times with ether. The ether extracts were combined with the organic layer, the whole dried over magnesium sulfate, the ether distilled off, and the obtained crystals separated on a porous filter, followed by washing and chloroform and petroleum ether. We obtained 3.3 g (40%) of α-bromo-β-ketobutyraldehyde with m.p. 108.5-109.5°. The melting point was not depressed when the compound was mixed with that obtained by the bromination of acetylacetaldehyde acetal in water (see above).

2-Amino-5-acetyloxazole. A mixture of 1.1 g of α-bromo-β-ketobutyraldehyde and 1 g of urea in 32 ml of acetone was heated for 45 minutes on the water bath. The precipitate had dissolved completely by the end of reaction. Most of the acetone was distilled off, after which the oily precipitate was poured into 150 ml of water and made alkaline with ammonia. After evaporating most of the water, the obtained crystalline precipitate was filtered, dissolved in a small amount of dilute hydrochloric acid, the solution filtered, and the filtrate cautiously made alkaline with ammonia. The obtained yellow precipitate was separated, and then washed with alcohol and ether. Evaporation of the mother liquor gave an additional amount of the substance. Yield 0.32 g (53%). After sublimation in vacuo, m.p. 210-211.5°.

Found %: C 47.19, 47.24; H 5.33, 5.29. $C_5H_6O_2N_2$. Calculated %: C 47.56; H 4.86.

Colorless crystals, readily soluble in most organic solvents. The compound turns dark when stored for a long time.

2-Amino-5-propionyloxazole. Obtained in a similar manner as the above from 1.63 g of α-bromo-β-ketovaleraldehyde and 1.1 g of urea in 35 ml of acetone. Yield 0.6 g (60%). The substance after sublimation had m.p. 164.5-166°.

Found %: N 20.13, 20.04. $C_6H_8O_2N_2$. Calculated %: N 19.99.

2-Amino-5-acetylthiazole. A solution of 2 g of α-bromo-β-ketobutyraldehyde in 35 ml of absolute alcohol was mixed with a solution of 0.9 g of thiourea in 40 ml of alcohol. When mild heat evolution had ceased the mixture was heated for 5-10 minutes at 60-70°, and here it assumed a dark red color. Then the alcohol was vacuum-distilled, and the obtained crystals were filtered and treated with sodium carbonate solution. The alkaline solution was immediately extracted with ether several times. The extracts were dried over sodium sulfate, the ether was distilled off, and the obtained crystals were filtered and recrystallized from alcohol. Yield 2.7 g (90%), m.p. 176-178°.

Found %: N 19.92, 19.73. $C_5H_6ON_2S$. Calculated %: N 19.72.

Yellow crystals, soluble in most organic solvents. The substance is stable to storage.

2-Amino-5-propionylthiazole. Obtained in a similar manner from 3 go of α-bromo-β-ketoisovaleraldehyde and 1.3 g of thiourea in 65 ml of alcohol. Yield 2.1 g (80%). After recrystallization from alcohol, m.p. 148-150°.

Found %: C 45.98, 46.18; H 5.10, 5.21; S 20.37. $C_6H_8ON_2S$. Calculated %: C 46.13; H 5.13; S 20.51.

5-Acetylthiazole. A solution of 2.5 g of α-bromo-β-ketobutyraldehyde in 100 ml of absolute ether was added to a solution of 2.2 g of technical thioformamide [14] in 15 ml of ether. After heating on the water for 30 minutes the reaction mixture was allowed to stand overnight, after which the ether was distilled off, the residue made alkaline, and the alkaline solution repeatedly extracted with ether. The extracts were dried over sodium sulfate, the ether was distilled off, and the residual oil was allowed to stand in the refrigerator to crystallize. The crystals were filtered, while the filtrate was extracted with hexane, from which some additional material was isolated by freezing. The total yield of 5-acetylthiazole was 0.3 g (15%). After recrystallization from petroleum ether the compound had m.p. 64.5-65.5°.

Found %: N 11.21, 11.17. C_5H_5ONS. Calculated %: N 11.02.

Colorless crystals, readily soluble in alcohol, benzene and ether, and difficultly soluble in petroleum ether and ligroin.

2-Phenyl-5-acetylthiazole. A solution of 4.5 g of α-bromo-β-ketobutyraldehyde in 30 ml of alcohol was added to a solution of 3.7 g of thiobenzamide in 10 ml of alcohol, and the mixture heated on the water bath for 3 hours. After conventional workup, we isolated 2.2 g (40%) of 2-phenyl-5-acetylthiazole with m.p. 148.5-150° (from alcohol).

Found %: N 6.68, 6.74. $C_{11}H_9ONS$. Calculated %: N 6.88.

Colorless crystals, readily soluble in benzene, moderately soluble in chloroform and alcohol, and difficultly soluble in hexane.

Oxidation of 5-Acetylthiazole With Potassium Permanganate. Into a flask, fitted with an efficient stirrer, was charged 0.1 g of 5-acetylthiazole in 30 ml of water and then 1 g of potassium permanganate was added in portions, with stirring, in 20 minutes. The reaction mixture was heated for 20 minutes to 70°, after which it was stirred for some time at room temperature. The mixture was filtered and extracted with ether, while the filtrate was acidified, and then extracted repeatedly with ether. After removal of the ether by distillation the crystalline precipitate was precipitated from sodium carbonate solution with acid, and then dried in a desiccator, after which it had m.p. 196.5-197.5°. Literature [15] for 5-thiazolecarboxylic acid: m.p. 196-197°.

2-Methylnaphtho [1, 2: 5', 6'] Pyrylium Chloroferrate. To 0.4 g of β-ketobutyraldehyde ethylene acetal were added in succession a solution of 0.5 g of β-naphthol in 5 ml of glacial acetic and a solution of 3.3 g of ferric chloride in 5 ml of conc. hydrochloric acid. A precipitate began to deposit immediately. After a day the crystals were suction-filtered, washed with acetic acid, then with absolute ether, and recrystallized from glacial acetic acid. Yield 0.5 g (50%). Green needles with m.p. 151-152°. Literature [13]: m.p. 151.5-152°. The mixed melting point with an authentic specimen was not depressed.

2-Methyl-3-bromonaphtho [1, 2: 5', 6'] Pyrylium Chloroferrate. To 0.93 g of β-naphthol in 5 ml of glacial acetic acid and a solution of 3.3 g of ferric chloride in 5 ml of concd. hydrochloric acid. The mixture soon began to deposit crystals of the pyrylium salt, which were filtered after two days. After conventional work-up, we obtained 0.6 g (32%) of compound with m.p. 203-205°.

Found %: C 35.79, 35.92; H 2.34, 2.41. $C_{14}H_{10}OCl_4BrFe$. Calculated %: C 35.71; H 2.13.

Green needles, difficultly soluble in ether, and moderately soluble in acetic acid. The substance is stable to storage.

SUMMARY

1. A method was developed for the synthesis of α-bromo-β-keto aldehydes by the bromination of β-keto aldehydes in aqueous medium in the presence of barium carbonate.

2. A method was developed for the synthesis of α-bromo-β-ketoaldehyde ethylene acetals by the bromination of β-ketoaldehyde ethylene acetals in ether in the presence of barium carbonate.

3. 2-Amino-5-acyloxazoles were obtained by the condensation of α-bromo-β-keto aldehydes with urea, while 2-substituted 5-acylthiazoles were obtained by the condensation of the indicated aldehydes with thiourea and thioamides. In this manner it was shown that α-bromo-β-keto aldehydes react as α-bromo aldehydes in the studied reactions.

4. The reaction of α-bromo-β-ketoaldehyde ethylene acetals with β-naphthol in the presence of ferric chloride and hydrochloric acid yields 2-alkyl-3-bromonaphtho [1, 2: 5', 6'] pyrylium salts.

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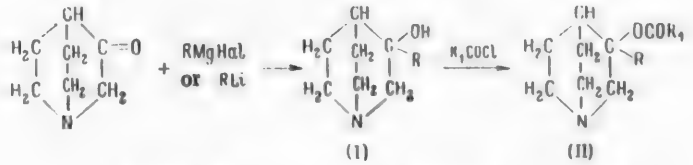
SYNTHESIS OF 3-HYDROXY-3-ALKYL(ARYL)QUINUCLIDINES AND THEIR ESTERS

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A systematic study of various substituted quinuclidine derivatives, conducted in our laboratory over a number of years, has made it possible to show that some of the 2-mono- and 2,3-disubstituted derivatives of quinuclidine possess high biological activity [1, 2]. The biological properties of 3-substituted quinuclidine derivatives have been studied in lesser detail. Only the spasmolytic activity of some esters of 3-hydroxyquinuclidine, shown in [3], should be mentioned here.

For the purpose of making a broader study of 3-substituted quinuclidine derivatives, we synthesized a number of 3-hydroxy-3-alkyl(aryl)quinuclidines and their esters. 3-Quinuclidone was used as the starting material for obtaining the 3-hydroxy-3-alkyl(aryl)quinuclidines. This ketone was converted to 3-hydroxy-3-alkyl(aryl)quinuclidines (I) when reacted with organomagnesium compounds. In some cases much better yields of the tertiary alcohols were obtained if organolithium compounds were used instead of organomagnesium compounds. Thus, the reaction of 3-quinuclidone with methylmagnesium iodide gave a 27% yield of 3-hydroxy-3-methylquinuclidine, whereas when the reaction was run with methyllithium the yield of tertiary alcohol was 81%.



(I)

(I) { R = CH_3 (a); R = C_2H_5 (b); R = CH_2—CH=CH_2 (c); R = C_5H_{11}-iso (d); R = C_6H_5 (e); R = $C_{10}H_7$ (f); R = $C_6H_5CH_2$ (g)

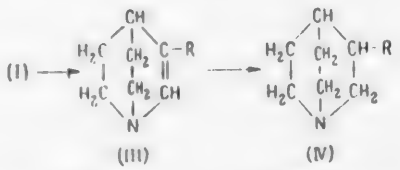
(II)

(II) { R = CH_3, R_1 = CH_3 (a); R = CH_3, R_1 = C_2H_5 (b); R = C_2H_5, R_1 = C_2H_5 (c); R = C_6H_5, R_1 = CH_3 (d); R = C_6H_5, R_1 = C_2H_5 (e).

The 3-hydroxy-3-alkyl(aryl)quinuclidines were converted to the esters (II) by heating the corresponding tertiary alcohols with acid chlorides. The best results were obtained when the reaction was run in chloroform. The esterification did not go to completion when the components were heated in benzene, and we found that the obtained reaction mixture of ester and starting alcohol could not be separated. The long heating of 3-phenyl-3-hydroxyquinuclidine (Ie) with acid chlorides (benzoyl and propionyl chlorides) in the absence of a solvent gave, instead of the expected esters, 3-phenyl-1-azabicyclo [2,2,2] oct-2-ene (IIIa). The ease with which 3-phenyl-3-hydroxyquinuclidine (Ie) was converted under the indicated conditions to unsaturated compound (IIIa) caused us to study the action of other water-removing agents on 3-hydroxy-3-alkyl(aryl)quinuclidines. As components, capable of cleaving water, we selected thionyl chloride and sulfuric acid. It was found that when 3-phenyl-3-hydroxyquinuclidine (Ie) was heated for a long time with approximately 15 moles of thionyl chloride, it was converted to a difficultly separable mixture of 3-phenyl-1-azabicyclo [2,2,2] oct-2-ene (IIIa) and 3-phenyl-3-chloroquinuclidine. The heating of this mixture with alcoholic KOH solution led to only one substance, namely 3-phenyl-1-azabicyclo [2,2,2] oct-2-end (IIIa), which is formed as the result of the 3-phenyl-3-chloroquinucli-

dine, present in the mixture, being converted to unsaturated compound (IIIa). The heating of 3-phenyl-3-hydroxyquinuclidine (Ie) with 70% sulfuric acid gave unsaturated compound (IIIa) in about 90% yield.

3-Methyl-3-hydroxyquinuclidine (Ia) behaves somewhat differently with the indicated water-removing agents. (Ia) remains unchanged when heated with 70% sulfuric acid, while treatment with 80% sulfuric acid leads to complete tarring of the compound. Short heating of 3-methyl-3-hydroxyquinuclidine (Ia) with the molecular amount of thionyl chloride in benzene is accompanied by the exclusive formation of 3-methyl-1-azabicyclo [2,2,2] oct-2-ene (IIIb).



(I) (III) (IV)

III and IV { R = C_6H_5 (a); R = CH_3 (b)

Reduction of unsaturated compounds (III) in the presence of platinum catalyst (Adams method) yields 3-alkyl(aryl)quinuclidines (IV).

Based on the best data obtained by the Pharmacological Section of the All-Union Chemicopharmaceutical Research Institute, the esters of 3-hydroxy-3-alkyl(aryl)quinuclidines proved to have little activity as choline and spasmolytic agents.

EXPERIMENTAL

3-Methyl-3-hydroxyquinuclidine (Ia). a) A solution of 13 g of methyl iodide in 30 ml of dry ether was added to a suspension of 2.16 g of magnesium in 20 ml of dry ether at such a rate that the ether boiled gently. Then the reaction mass was heated for another hour at ether boil to effect complete solution of the magnesium. After this the mixture was cooled to -10°, and a solution of 5 g of 3-quinuclidone in 30 ml of ether was added gradually with stirring, maintaining the temperature between -7 and -10°. The reaction mass was allowed to stand for 18 hours at -5°. Then 70 ml of 12% hydrochloric acid was added, and the ether layer was separated and washed with 12% hydrochloric acid solution. The combined hydrochloric acid extracts were evaporated on the water bath to a small volume, treated with 50% potassium carbonate solution, the inorganic salts suction-filtered, and the alkaline filtrate extracted with chloroform. The chloroform solution was dried over potassium carbonate, the solvent vacuum-distilled, and the residue ground with 30 ml of ether, and 1 g of a tarry mass separated. The ether solution was evaporated to a volume of 10 ml, and cooling of the residue gave crystals of 3-methyl-3-hydroxyquinuclidine. The product was filtered and washed with ether to give 1.53 g (27%) of substance. M.p. 108-110°. From [5]: m.p. 109-111°. After separating the 3-methyl-3-hydroxyquinuclidine, we recovered 1.2 g of 3-quinuclidone from the ether mother liquor.

b) A solution of 28.7 g of methyl iodide in 30 ml of ether was added with stirring to 2.8 g of finely cut lithium, immersed in 70 ml of dry ether, with maintenance of a gentle ether boil during the addition. Then the reaction mass was kept at same temperature for another 2 hours, after which it was cooled to 5°, and a solution of 10 g of 3-quinuclidone in 100 ml of dry benzene was added, keeping the temperature of the mixture between 5 and 10°. Then the mixture was allowed to stand at room temperature for 15-18 hours; at the end of this time 30 ml of water was added, then 50 ml of 50% KOH solution, and the alkaline solution was extracted with benzene. The benzene solution was dried over potassium carbonate, and the residue, after distilling off the benzene, was recrystallized from 50 ml of ethyl acetate. We obtained 9.2 g (81.2%) of 3-methyl-3-hydroxyquinuclidine. M.p. 108-110°.

3-Methyl-1-azabicyclo [2,2,2] oct-2-ene (IIIb). A mixture of 1.2 g of 3-methyl-3-hydroxyquinuclidine hydrochloride, 1 g of thionyl chloride and 12 ml of dry benzene was heated at 55-60° for 7 hours. Here all of the solid went into solution. The benzene was vacuum-distilled, while the residue was dissolved in 5 ml of anhydrous alcohol, and the alcohol solution was treated with 30 ml of ether. The obtained crystals were filtered and washed with ether. We obtained 0.9 g (83.7%) of 3-methyl-1-azabicyclo [2,2,2] oct-2-ene hydrochloride. M.p. 251-253° (from alcohol).

Found %: C 61.17; H 9.26; N 8.75; Cl 22.06. $C_8H_{13}N \cdot HCl$. Calculated %: C 60.73; H 8.82; N 8.77; Cl 22.30.

3-Methylquinuclidine (IVb). A solution of 3-methyl-azabicyclo [2.2.2] oct-2-ene hydrochloride in 30 ml of anhydrous alcohol was shaken with hydrogen in the presence of 0.1 g of platinum oxide (Adams method). After the calculated amount of hydrogen had been absorbed, the platinum black was filtered, and the alcohol solution was evaporated in vacuo. We obtained 1.3 g (86.6%) of 3-methylquinuclidine hydrochloride. M.p. 312-314°. According to [6], m.p. 312-324°.

3-Ethyl-3-hydroxyquinuclidine (Ib). Ethylmagnesium bromide was prepared by reacting 1.75 g of magnesium with 7.85 g of ethyl bromide in 45 ml of dry ether. An ether solution of 3 g of 3-quinuclidone in 35 ml of ether was added to the ether solution of ethylmagnesium bromide at -8 to -10°. Then the reaction mass was kept at room temperature for 40 hours, after which it was heated in succession with 10 ml of water and 20 ml of 17% hydrochloric acid. The ether layer was separated, while the hydrochloric acid solution was treated with 50 ml of 50% KOH solution, and then extracted with benzene. The benzene solution was dried over potassium carbonate, the benzene was vacuum-distilled, and the residue was recrystallized from 15 ml of anhydrous ethyl acetate. We obtained 1.4 g (37.7%) of 3-ethyl-3-hydroxyquinuclidine as colorless crystals, readily soluble in alcohol, acetone and chloroform, more difficultly soluble in water, and insoluble in ether. M.p. 109-111°.

Found %: C 69.53, 70.00; H 11.13, 11.04. $C_9H_{17}ON$. Calculated %: C 69.68; H 10.97.

3-Allyl-3-hydroxyquinuclidine (Ic). A solution of 3 g of 3-quinuclidone in 30 ml of ether was added at -8 to -10°, with stirring, to a solution of allylmagnesium bromide in 70 ml of dry ether, prepared from 1.75 g of magnesium and 8.7 g of allyl bromide. The reaction mass was kept at room temperature for 20 hours, and then it was heated at the boil for 3 hours. After treatment, similar to that described in the previous experiment, the alkaline solution was extracted with benzene. The benzene extract was dried over potassium carbonate, the benzene was distilled off, and the residue was heated in a vacuum (10-12 mm); here 2 g of sublimed 3-quinuclidone was obtained. The substance, obtained after removal of the 3-quinuclidone, was vacuum-distilled twice. We obtained 0.5 g of 3-allyl-3-hydroxyquinuclidine as a viscous yellow liquid, readily soluble in organic solvents, and difficultly soluble in water. B.p. 126-130° (0.3 mm).

Found %: C 71.29; H 9.96. $C_{10}H_{17}ON$. Calculated %: C 71.85; H 10.18.

3-Isoamyl-3-hydroxyquinuclidine (Id). A solution of 3 g of 3-quinuclidone in 30 ml of ether was added at 0-2°, with stirring, to a solution of isoamylmagnesium bromide in 40 ml of anhydrous ether, obtained from 9.05 g of isoamylbromide and 1.46 g of magnesium. The reaction mass was then worked up as described above. The alkaline solution was extracted with chloroform. The chloroform extract was dried over potassium carbonate, the chloroform was vacuum-distilled, and the residue was sublimed to give 1.5 g of 3-quinuclidone. The viscous liquid, obtained after removal of the 3-quinuclidone, was ground with 10 ml of water, and the obtained crystals were separated, washed with water, dried, and then recrystallized from ether, using charcoal. We obtained 0.3 g of 3-isoamyl-3-hydroxyquinuclidone. M.p. 107-110°.

Found %: C 72.90, 73.09; H 11.69, 11.76; N 7.15, 7.37. $C_{12}H_{23}ON$. Calculated %: C 73.10; H 11.67; N 7.10.

The hydrochloride was obtained as colorless crystals, m.p. 192-194°.

3-Phenyl-3-hydrocyquinuclidine (Ie). A solution of 14 g of 3-quinuclidone in 80 ml of ether was added at 5°, with stirring, to a solution of phenyllithium in 90 ml of dry ether, obtained from 1.96 g of lithium and 22.3 g of bromobenzene. The mixture was kept at room temperature for 15 hours, then heated at the boil for 2 hours, cooled to room temperature, and treated with 25 ml of water. The obtained precipitate was filtered, and washed on the filter with water, and then with ether. We obtained 17.32 g (76.4%) of 3-phenyl-3-hydroxyquinuclidine as colorless crystals, readily soluble in alcohol, less readily soluble in ethyl acetate and benzene, and insoluble in ether and water. M.p. 164-166°* (from a mixture of alcohol and ethyl acetate).

Found %: C 76.75; H 8.30; N 6.94. $C_{13}H_{17}ON$. Calculated %: C 76.85; H 8.37; N 6.90.

The hydrochloride was obtained as colorless crystals, m.p. 217-219°.

*When the present study had been completed and was ready to be published, a communication [4] appeared in which the preparation of 3-phenyl-3-hydroxyquinuclidine was described.

3-Phenyl-1-azabicyclo [2.2.2] oct-2-ene (IIIa). a) A mixture of 1 g of 3-phenyl-3-hydroxyquinuclidine, 5 ml of thionyl chloride and 12 ml of dry benzene was heated for 3 hours at 55-60°. The benzene and excess thionyl chloride were vacuum-distilled. The residue was treated with 10 ml of 50% potassium carbonate solution, and the alkaline solution was extracted with chloroform. The chloroform solution was dried over sodium sulfate. The oily substance, obtained after distilling off the chloroform, gave a positive test for both halogen and double bond. This substance was apparently a mixture of 3-phenyl-1-azabicyclo [2.2.2] oct-2-ene and 3-phenyl-3-chloroquinuclidine. To cleave hydrogen chloride from the latter, the obtained substance was treated with a solution of 0.12 g of KOH in 3 ml of anhydrous alcohol, and the reaction mass was heated at the boil for 5 hours. The cooled mixture, containing a precipitate of potassium chloride, was treated with an alcohol solution of hydrogen chloride until it showed acid to Congo. The potassium chloride was suction-filtered, the alcohol was vacuum-distilled, and the residue was treated with 50% potassium carbonate solution, and then extracted with ether. The ether extract was dried over potassium carbonate, the ether was distilled off, and the substance was vacuum-distilled. We obtained 0.4 g (52.6%) of 3-phenyl-1-azabicyclo [2.2.2] oct-2-ene as a colorless mobile liquid, readily soluble in water and in organic solvents. B.p. 105-108° (0.35 mm).

Found %: N 7.61, 7.82. $C_{13}H_{15}N$. Calculated %: N 7.57.

b) A mixture of 2 g of 3-phenyl-3-hydroxyquinuclidine and 2 ml of freshly distilled propionyl chloride was heated at 80° for 10 hours. The cooled solution was treated with 15 ml of dry ether, and the obtained precipitate was separated, washed with ether, and dried. We obtained 1.65 g (75.7%) of 3-phenyl-1-azabicyclo [2.2.2] oct-2-ene hydrochloride. Colorless crystals, readily soluble in water, alcohol and acetone, and insoluble in ethyl acetate, ether and benzene. M.p. 211-212° (from a mixture of acetone and ether).

Found %: C 70.63, 70.43; H 7.36, 6.70; N 6.13; Cl 15.93. $C_{13}H_{15}N \cdot HCl$. Calculated %: C 70.42; H 7.23; N 6.32; Cl 16.03.

c) A solution of 1.5 g of 3-phenyl-3-hydroxyquinuclidine in 3 ml of 70% sulfuric acid was heated on the boiling water bath for 5 hours. The solution gradually assumed a dark brown color. At the end of heating, the reaction mass was cooled, diluted with 5 ml of water, made alkaline with 50% potassium carbonate solution, and extracted with ether. The ether solution was dried over potassium carbonate, the ether distilled off, and the residue vacuum-distilled. We obtained 1.2 g (87.6%) of 3-phenyl-1-azabicyclo [2.2.2] oct-2-ene. B.p. 106-108° (0.35 mm).

The hydrochloride had m.p. 211-212°, and did not depress the melting point when mixed with the substance obtained by method "b".

3-Phenylquinuclidine (IVa). To a solution of 1.15 g of 3-phenyl-1-azabicyclo [2.2.2] oct-2-ene in 30 ml of anhydrous alcohol was added 0.1 g of platinum oxide (Adams method), and the mixture was shaken with hydrogen. When the calculated amount of hydrogen had been absorbed (130 ml), the platinum black was filtered, the alcohol solution was evaporated in vacuo, and the residue was diluted with a small amount of ether, and the crystals filtered. We obtained 1 g (86.7%) of 3-phenylquinuclidine hydrochloride. Colorless crystals, readily soluble in alcohol and water, difficultly soluble in acetone, and insoluble in ether, benzene and ethyl acetate. M.p. 189-191° (from a mixture of acetone and alcohol).

Found %: N 6.01, 6.10; Cl 15.63, 15.70. $C_{13}H_{17}N \cdot HCl$. Calculated %: 6.26; Cl 15.88.

The free 3-phenylquinuclidine was isolated by treating 3-phenylquinuclidine hydrochloride with potassium carbonate. 3-Phenylquinuclidine was obtained as a colorless mobile liquid, soluble in organic solvents and in water. B.p. 114° (0.3 mm).

Found %: N 7.40. $C_{13}H_{17}N$. Calculated %: N 7.48.

3-(α-Naphthyl)-3-hydroxyquinuclidine (If). A solution of 5 g of 3-quinuclidone in 50 ml of ether was added at 2-3°, with stirring, to the naphthylmagnesium bromide, prepared from 20.7 g of α-bromo-naphthalene, 2.43 g of magnesium and 60 ml of dry ether. The reaction mass, after treating as described in previous experiments, was treated with 50 ml of 17% hydrochloric acid, the mixture stirred until the precipitate dissolved, after which the hydrochloric acid layer was separated and extracted with ether until all of the naphthalene had been removed. Then the hydrochloric acid solution was treated with 50% potassium carbonate solution, and the obtained precipitate was separated, washed with water, and dried. The dry precipitate was extracted with hot chloro-

form, the chloroform solution was evaporated in vacuo, and the residue was dissolved in 80 ml of alcohol. The alcohol solution was decolorized with charcoal, filtered, and evaporated to a volume of 10 ml. The obtained crystals were separated, washed with a small amount of alcohol, and dried. We obtained 3.3 g of 3-(α-naphthyl)-3-hydroxyquinuclidine as colorless crystals, readily soluble in acetone, alcohol and chloroform, and insoluble in ether, benzene and water. M.p. 224-226° (from alcohol).

Found %: C 80.38, 80.25; H 7.38, 7.42; N 5.39, 5.21. $C_{17}H_{19}ON$. Calculated %: C 80.62; H 7.51; N 5.53.

3-Benzyl-3-hydroxyquinuclidine (Ig). A solution of 3 g of 3-quinuclidone in 30 ml of ether was added to a solution of benzylmagnesium chloride in 35 ml of dry ether, obtained from 7.6 g of benzyl chloride and 1.46 g of magnesium. The reaction was run the same as in the previous experiment. After decomposing the Grignard complex with hydrochloric acid, the hydrochloric acid solution was treated with 50% potassium carbonate solution, and then extracted with chloroform. The chloroform solution was dried over sodium sulfate, the chloroform was distilled off, and the solid residue was recrystallized from a mixture of 30 ml of acetone and 15 ml of alcohol. We obtained 2.15 g of 3-benzyl-3-hydroxyquinuclidine. Colorless crystals, soluble in alcohol, and insoluble in water, ether, acetone and ethyl acetate. M.p. 175-177°.

Found %: C 77.71, 77.43; H 8.87, 9.03; N 6.24, 6.23. $C_{14}H_{19}ON$. Calculated %: C 77.42; H 8.76; N 6.45.

3-Methyl-3-acetoxyquinuclidine. A suspension of 1.5 g of 3-methyl-3-hydroxyquinuclidine in 15 ml of anhydrous chloroform was treated with 2 ml of freshly distilled acetyl chloride. Here heat was evolved and the precipitate went into solution. The reaction mass was allowed to stand at room temperature until the next day, after which it was heated at the boil for 2 hours, and then the chloroform was vacuum-distilled. The residue was dissolved in 10 ml of water, then 10 ml of 50% potassium carbonate solution was added, and the alkaline solution was extracted with ether. The ether extract was dried over potassium carbonate, the ether evaporated, and the residue was distilled. We obtained 1.5 g (79%) of 3-methyl-3-acetoxyquinuclidine as a colorless mobile liquid, readily soluble in water and in organic solvents. B.p. 65-66° (0.4 mm).

The hydrochloride was obtained as colorless crystals, m.p. 193-195° (from a mixture of acetone and alcohol).

Found %: C 54.75; H 8.38; N 6.38; Cl 16.17. $C_{10}H_{17}O_2N \cdot HCl$. Calculated %: C 54.67; H 8.20; N 6.38; Cl 16.17.

3-Methyl-3-propionyloxyquinuclidine (IIb). A solution of 1 g of 3-methyl-3-hydroxyquinuclidine in 10 ml of anhydrous chloroform was treated with 1.2 ml of freshly distilled propionyl chloride. The reaction was run in the same manner as described in the previous experiment. We obtained 1.15 g (82.2%) of the ester as a colorless mobile liquid, readily soluble in water and in organic solvents. B.p. 75-76° (0.3 mm).

The hydrochloride was obtained as colorless crystals. M.p. 176-178° (from acetone).

Found %: C 57.17; H 8.51; N 5.63; Cl 15.21. $C_{10}H_{19}O_2N \cdot HCl$. Calculated %: C 56.63; H 8.56; N 6.00, Cl 15.20.

3-Ethyl-3-propionyloxyquinuclidine (IIc). The reaction mass, composed of 1 g of 3-ethyl-3-hydroxyquinuclidine, 1.5 ml of propionyl chloride and 10 ml of anhydrous chloroform, was treated the same as described above. We obtained 1.08 g (79.5%) of the ester as a colorless mobile liquid, readily soluble in water and in organic solvents. B.p. 86-87° (0.45 mm).

The hydrochloride was obtained as colorless crystals, m.p. 201-203° (from a mixture of acetone and alcohol).

Found %: N 5.75, 5.31; Cl 14.24, 14.28. $C_{12}H_{21}O_2N \cdot HCl$. Calculated %: N 5.66; Cl 14.35.

3-Phenyl-3-acetoxyquinuclidine (IId). A mixture of 1 g of 3-phenyl-3-hydroxyquinuclidine, 1 ml of acetyl chloride and 5 ml of chloroform was kept at room temperature for 48 hours, after which it was heated at the boil for 2 hours. The reaction mass was then cooled, and the precipitate was filtered, washed on the filter with chloroform and with ether, and recrystallized from anhydrous alcohol. We obtained 1.38 g (85.7%) of 3-phenyl-3-acetoxyquinuclidine hydrochloride, containing a molecule of crystallization alcohol. Colorless crystals, readily soluble in water and in alcohol. M.p. 192-193°.

Found %: C 61.85; H 7.76; N 4.23; Cl 10.81. $C_{15}H_{19}O_2N \cdot HCl \cdot C_2H_5OH$. Calculated %: C 62.29; H 7.95; N 4.27; Cl 10.84.

3-Phenyl-3-propionyloxyquinuclidine (IIe). A suspension of 2 g of 3-phenyl-3-hydroxyquinuclidine in 20 ml of anhydrous chloroform was treated with 3 ml of propionyl chloride. The mixture was kept at room temperature for 24 hours, after which it was heated for 4 hours at the boil, then cooled, and the unreacted 3-phenyl-3-hydroxyquinuclidine was separated. The chloroform solution was evaporated in vacuo, and the remainder of the treatment was the same as described for the preparation of 3-methyl-3-acetoxyquinuclidine. The yield of 3-phenyl-3-propionyloxyquinuclidine was 1.83 g (74.7%), b.p. 148° (0.25 mm). Colorless viscous liquid, readily soluble in organic solvents, and less readily soluble in water.

Found %: C 74.59, 74.46; H 8.00, 8.30; N 5.49. $C_{16}H_{21}O_2N$. Calculated %: C 74.13; H 8.10; N 5.41.

The hydrochloride was obtained as colorless crystals, m.p. 176-178°.

SUMMARY

Starting with 3-quinuclidone, we prepared a number of 3-hydroxy-3-alkyl(aryl)quinuclidines and their esters. It was shown that 3-hydroxy-3-alkyl(aryl)quinuclidines, when reacted with different reagents like acid chlorides, sulfuric acid and thionyl chloride, are easily transformed into 3-alkyl(aryl)-1-azabicyclo [2,2,2] oct-2-enes. The latter on reduction yield 3-alkyl(aryl)-1-azabicyclo [2.2.2] oct-2-enes. The latter on reduction yield 3-alkyl(aryl)quinuclidines.

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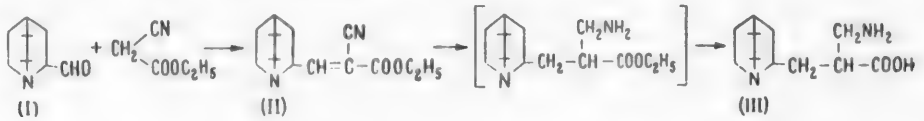
AMINO ACIDS OF THE QUINUCLIDINE SERIES

L. N. Yakhontov and M. V. Rubtsov

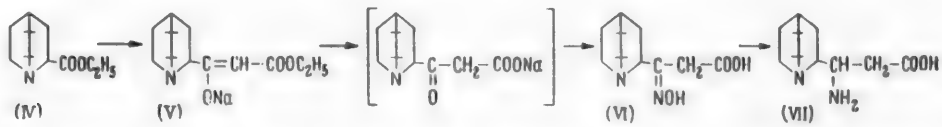
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Biological studies of some analogs of natural heterocyclic amino acids (histidine, trypotophan, etc.) have revealed that changing the structure of the amino acid, including replacement of one heterocyclic moiety by another, leads in a number of cases to antagonists, or antimetabolites, for vitagenic amino acids [1]. In connection with this it seemed of interest to study the biological activity of those amino acids in which the heterocyclic moiety is the bicyclic quinuclidine system. Data on either the preparation or biological activity of amino acids of the quinuclidine series are absent in the literature.

In this paper we discuss the synthesis of three amino acids that are quinuclidine derivatives: α-aminomethyl-β-(2-quinuclidinyl)propionic acid (III), β-(2-quinuclidinyl)-β-aminopropionic acid (VII) and 3-amino-2-quinuclidinecarboxylic acid (XII). We used 2-formylquinuclidine (I) [2] as the starting material for the synthesis of α-aminomethyl-β-(2-quinuclidinyl)propionic acid (III).

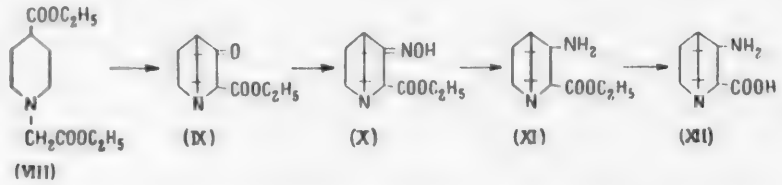


The Knoevnagel condensation of aldehyde (I) with cyanoacetic ester led to obtaining the ethyl ester of β-(2-quinuclidinyl)-α-cyanoacrylic acid (II) in nearly quantitative yield. Simultaneous reduction of the double bond and cyano group in compound (II) was effected by hydrogenation in the presence of platinum catalyst (Adams method). Without being isolated, the obtained ethyl α-aminomethyl-β-(2-quinuclidinyl)propionate was saponified to α-aminomethyl-β-(2-quinuclidinyl)propionic acid (III). We synthesized β-(2-quinuclidinyl)-β-aminopropionic acid (VII) by starting with the ethyl ester of 2-quinuclidinecarboxylic acid (IV).



As we had already reported earlier [3], the Claisen condensation of ethyl 2-quinuclidinecarboxylate with ethyl acetate yields the readily isolated sodium derivative of the enol form of the ethyl ester of β-(2-quinuclidinyl)-β-ketopropionic acid (V). Compound (V) is difficultly soluble in water, but if allowed to stand with water for a day at room temperature it gradually goes into solution. Here the ester group is saponified with formation of the sodium salt and transformation of the enol group to the keto group. The end result is a water solution of the sodium salt of β-(2-quinuclidinyl)-β-ketopropionic acid. The oxime (VI) of this keto acid was obtained by reacting equimolar amounts of the sodium salt and hydroxylamine hydrochloride in anhydrous alcohol medium. Reduction of oxime (VI) with platinum catalyst (Adams method) led to its conversion to β-(2-quinuclidinyl)-β-aminopropionic acid (VII).

In contrast to both of the above described amino acids, where both the carboxyl and amino groups are found in the side chain, in the case of 3-amino-2-quinuclidinecarboxylic acid (XII) both the amino group and the carboxyl are present as substituents in the quinuclidine nucleus. Amino acid (XII) was synthesized by the following scheme:



Cyclization of the ethyl ester of 1-carbethoxymethylisonipecotic acid (VIII) by the Dieckmann method was effected under conditions similar to those described for the synthesis of 3-quinuclidone [4]. The cyclization product, being the potassium derivative of the enol form of the ethyl ester of 3-keto-2-quinuclidinecarboxylic acid, was treated with the calculated (based on the potassium metal taken for the cyclization) amount of 10% acetic acid, and then with an equivalent amount of solid potassium carbonate. After further salting out with sodium chloride, the ethyl ester of 3-keto-2-quinuclidinecarboxylic acid was extracted with chloroform. It should be mentioned that if instead of 10% acetic acid, mineral acids are used to acidify the solution, and also if an excess of either acetic acid or potassium carbonate is used, then the yield of keto ester (IX) is reduced substantially. The reaction of keto ester (IX) with hydroxylamine hydrochloride was run in boiling alcohol. Here the alkaline reagent, tying up the hydrogen chloride, is the ethyl 3-keto-2-quinuclidinecarboxylate itself. The reaction of equimolar amounts of keto ester (IX) and hydroxylamine hydrochloride gave the monohydrochloride of the oxime of the ethyl ester of 3-keto-2-quinuclidinecarboxylic acid (X) in 80% yield. Reduction of oxime (X) with platinum catalyst (Adams method), followed by saponification of the ester group, gave 3-amino-2-quinuclidinecarboxylic acid in excellent yield.

It should be mentioned that the three amino acids synthesized by us each have two asymmetric carbon atoms, and consequently it could be expected that the diastereoisomeric amino acids would be obtained. However, in all cases, we obtained only one diastereoisomer in high yield. This is apparently due to the stereospecificity of the hydrogenation in the presence of platinum catalyst.

EXPERIMENTAL

Ethyl Ester of β-(2-Quinuclidinyl)-α-cyanoacrylic Acid. A solution of 1.1 g of freshly prepared 2-formylquinuclidine and 0.9 g of cyanoacetic ester in 3 ml of anhydrous pyridine was treated with 5 drops of piperidine. The reaction mass was allowed to stand at room temperature for 10 days. The obtained crystalline precipitate was filtered and washed with alcohol. We obtained 0.1 g of ethyl β-(2-quinuclidinyl)-α-cyanoacrylate with m.p. 139.5-141°. The pyridine was vacuum-distilled, and the residue was washed with alcohol. We obtained another 1.7 g of ethyl β-(2-quinuclidinyl)-α-cyanoacrylate with m.p. 139.5-141°. The total yield was 1.8 g (97.2%). Colorless crystals, very difficultly soluble in water and the common organic solvents, readily soluble in mineral acids, and less readily soluble in pyridine. The compound gives a positive test with potassium permanganate for the double bond.

Found %: C 66.48, 66.38; H 7.59, 7.70; N 11.95, 11.97. $C_{13}H_{18}O_2N_2$. Calculated %: C 66.67; H 7.69; N 11.95.

The picrate was obtained as yellow crystals, m.p. 130.5-131° (from alcohol).

Found %: C 49.10, 49.28; H 4.49, 4.80; N 15.38. $C_{13}H_{18}O_2N_2 \cdot C_6H_3O_7N_3$. Calculated %: C 49.24; H 4.54; N 15.12.

α-Aminoethyl-β-(2-quinuclidinyl)propionic Acid. A solution of 0.1 g of ethyl β-(2-quinuclidinyl)-α-cyanoacrylate in 12 ml of a 6% solution of hydrogen chloride in anhydrous alcohol was hydrogenated in the presence of 0.1 g of platinum catalyst, prepared by the Adams method. The hydrogenation was run at room temperature and a pressure of 15-20 cm of water column. When the absorption of hydrogen had ceased, the catalyst was filtered, and the filtrate was evaporated in vacuo. The residue was dissolved in 1 ml of concentrated hydro-

chloric acid, and refluxed for 5 hours. The hydrochloric acid was distilled off, while the residue was dissolved in alcohol, and the solution then treated with an alcohol solution of picric acid to precipitate the dipicrate of α-aminomethyl-β-(2-quinuclidinyl)propionic acid as yellow crystals with m.p. 125° (decomp.). Yield 0.17 g (62%).

Found %: C 41.08; H 4.01; N 17.01. $C_{11}H_{20}O_2N_2 \cdot 2C_6H_3O_7N_3$. Calculated %: C 41.20; H 3.88; N 16.71.

Oxime of β-(2-Quinuclidinyl)-β-ketopropionic Acid. A mixture of 1.25 g of the sodium derivative of the enol form of ethyl β-(2-quinuclidinyl)-β-ketopropionate and 20 ml of water was allowed to stand at room temperature for a day. The precipitate gradually went into solution. The resulting homogeneous solution was evaporated in vacuo. We obtained 1.15 g of the sodium salt of β-(2-quinuclidinyl)-β-ketopropionic acid. M.p. 240° (decomp.). The obtained sodium salt was treated with 0.4 g of hydroxylamine hydrochloride and 10 ml of anhydrous alcohol. The reaction mass was stirred for 12 hours at 18-20°. The precipitate of sodium chloride was filtered. The alcohol solution was evaporated in vacuo. We obtained 1 g (93%) of the oxime of β-(2-quinuclidinyl)-β-ketopropionic acid as an oily substance, insoluble in ether and benzene, and soluble in water, alcohol and chloroform.

The dihydrochloride was obtained as colorless crystals, m.p. 284° (decomp.). The compound is soluble in water, and insoluble in the common organic solvents.

Found %: C 42.32, 42.41; H 6.40, 6.54; Cl' 24.94. $C_{10}H_{16}O_3N_2 \cdot 2HCl$. Calculated %: C 42.11; H 6.32; Cl' 24.91.

The picrate was obtained as yellow crystals, m.p. 167-170°.

Found %: C 43.29; H 4.23; N 15.72. $C_{10}H_{16}O_3N_2 \cdot C_6H_3O_7N_3$. Calculated %: C 43.53; H 4.30; N 15.87.

β-(2-Quinuclidinyl)-β-aminopropionic Acid. A solution of 0.9 g of the oxime of β-(2-quinuclidinyl)-β-ketopropionic acid in 30 ml of anhydrous alcohol was hydrogenated in the presence of 0.4 g of platinum catalyst, prepared by the Adams method. The hydrogenation was run at room temperature and a pressure of 20-30 cm of water column, and was ended in 4 hours. The catalyst was filtered, and the filtrate was treated with an alcohol solution of hydrogen chloride until it showed acid to Congo. The obtained crystalline precipitate of the dihydrochloride of β-(2-quinuclidinyl)-β-aminopropionic acid was filtered, and then washed with anhydrous alcohol and ether. The yield of β-(2-quinuclidinyl)-β-aminopropionic acid dihydrochloride was 0.8 g (78%). Colorless crystals with m.p. 283° (decompn.). The compound is readily soluble in water and in methanol, and is difficultly soluble in the other common organic solvents.

Found %: C 44.50, 44.20; H 7.24, 7.52; Cl' 26.03. $C_{10}H_{18}O_2N_2 \cdot 2HCl$. Calculated %: C 44.28; H 7.38; Cl' 26.19.

Ethyl Ester of 3-Keto-2-quinuclidinecarboxylic Acid. A solution of 60 g of ethyl 1-carbethoxymethylisonipecotate in 150 ml of anhydrous toluene was added gradually, in 1 hour, at 120° (oil bath), to the potassium ethylate, obtained from 24 g of potassium and 36 ml of anhydrous alcohol in 100 ml of anhydrous toluene. The reaction mass was heated under reflux, with stirring, for 5 hours. After cooling, the toluene was decanted, while the viscous deposit of the potassium derivative of the enol form of ethyl 3-keto-2-quinuclidinecarboxylate was washed 3 times with 50 ml portions of anhydrous ether, and then treated with 370 ml of 10% acetic acid. The acetic acid solution was neutralized with 85.1 g of potassium carbonate. After additional salting out with sodium chloride, the ethyl 3-keto-2-quinuclidinecarboxylate was extracted with chloroform. The chloroform solution was dried over fused potassium carbonate, and the solvent was vacuum-distilled. The crystalline residue was washed with anhydrous acetone (3 times with 10 ml portions), and then recrystallized from anhydrous acetone. We obtained 36.42 g (75%) of ethyl 3-keto-2-quinuclidinecarboxylate. Colorless crystals, m.p. 109-110°. The compound is readily soluble in water, alcohols, and chloroform, difficultly soluble in ether, benzene, acetone and toluene, and insoluble in petroleum ether.

Found %: C 60.60, 61.02; H 7.70, 7.50; N 7.31, 7.22. $C_{10}H_{15}O_3N$. Calculated %: C 60.91; H 7.61; N 7.10.

Hydrochloride of the Oxime of the Ethyl Ester of 3-Keto-2-quinuclidinecarboxylic Acid. A mixture of 2 g of ethyl 3-keto-2-quinuclidinecarboxylate and 0.7 g of hydroxylamine hydrochloride in 20 ml of anhydrous alcohol was heated under reflux for 4 hours. During reflux, the precipitate of hydroxylamine hydrochloride gradually dissolved. After some time, the hydrochloride of the oxime of ethyl 3-keto-2-quinuclidinecarboxylate began to

crystallize from the boiling alcohol. The crystalline precipitate was filtered. We obtained 1.8 g of colorless crystals, m.p. 196° (decomp.). The alcohol solution was evaporated to a volume of 5 ml. The resulting crystalline precipitate was filtered. We obtained another 0.36 g of substance with m.p. 196° (decomp.). The total yield of the hydrochloride of the oxime of ethyl 3-keto-2-quinuclidinecarboxylate was 2.16 g (80%). Colorless crystals, readily soluble in water, difficultly soluble in alcohols and in acetone, and insoluble in ether, chloroform, benzene and toluene.

Found %: C 48.25, 48.41; H 6.90, 6.87; N 11.11, 11.04; Cl' 14.62, 14.63. $C_{10}H_{16}O_3N_2 \cdot HCl$. Calculated %: C 48.29; H 6.84; N 11.26; Cl' 14.29.

Ethyl Ester of 3-Amino-2-quinuclidinecarboxylic Acid. A solution of 1.5 g of ethyl 3-keto-2-quinuclidinecarboxylate oxime hydrochloride in 30 ml of anhydrous alcohol was treated with 2 ml of a 30% alcohol solution of hydrogen chloride, and then hydrogenated in the presence of 0.1 g of platinum catalyst, prepared by the Adams method. The hydrogenation was run at room temperature and a pressure of 20-30 cm of water column, and was ended in 6 hours. The catalyst was filtered, and the filtrate was evaporated in vacuo. We obtained 1.65 g (99.4%) of ethyl 3-amino-2-quinuclidinecarboxylate dihydrochloride as colorless crystals. The compound is readily soluble in water and in alcohol, and is insoluble in the other common organic solvents. M.p. 185° (decomp.).

Found %: C 44.16, 44.02; H 7.33, 7.26; N 10.11, 10.42; Cl' 26.34. $C_{10}H_{18}O_2N_2 \cdot HCl$. Calculated %: C 44.28; H 7.38; N 10.33; Cl' 26.19.

3-Amino-2-quinuclidinecarboxylic Acid. A mixture of 1.1 g of ethyl 3-amino-2-quinuclidinecarboxylate dihydrochloride and 10 ml of concd. HCl was heated on the boiling water bath for 6 hours. The obtained solution was evaporated in a porcelain dish to dryness, and the residue was recrystallized from anhydrous alcohol. We obtained 0.9 g (91%) of the dihydrochloride of 3-amino-2-quinuclidinecarboxylic acid. Colorless crystals, m.p. 242° (decomp.). The compound is readily soluble in water, and is insoluble in the common organic solvents.

Found %: C 39.25, 39.32; H 6.64, 6.59; N 11.05, 11.40; Cl' 29.15, 29.32. $C_8H_{14}O_2N_2 \cdot 2HCl$. Calculated %: C 39.50; H 6.58; N 11.52; Cl 29.22.

SUMMARY

The following amino acids of the quinuclidine series were synthesized: α-aminomethyl-β-(2-quinuclidinyl)propionic acid, β-(2-quinuclidinyl)-β-aminopropionic acid, and 3-amino-2-quinuclidinecarboxylic acid.

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SYNTHESIS AND TRANSFORMATIONS OF ETHYLENIC α-GLYCOLS

VII. TRANSFORMATION OF 1,2,4-TRIPHENYL-3-BUTENE-1,2-DIOL AND 2,3-DIMETHYL-5-PHENYL-4-PENTENE-2,3-DIOL

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From recently published papers [1-3] it can be seen that ethylenic α-glycols, in acid medium, besides forming aldehydes and ketones, are also capable of isomerizing to substituted dihydrofurans. A conclusive decision as to the mechanism of this tranformation is still not possible from the available experimental material. For this reason we decided to run some experiments on the isomerization of still two other glycols: 1,2,4-triphenyl-3-butene-1,2-diol (I) and 2,3-dimethyl-5-phenyl-4-pentene-2,3-diol (II), in 20% alcoholic and 30% aqueous solutions of sulfuric acid, at temperatures ranging from 60 to 100°.

The heating of 1,2,4-triphenyl-3-butene-1,2-diol with 20% alcoholic H_2SO_4 solution at 60-70° gave a light-yellow oily substance, which from the properties and analysis data corresponded to an aldehyde of the ethylenic series. Oxidation of this aldehyde gave benzoic and diphenylacetic acids, which permitted assuming that it was 2,2,4-triphenyl-3-butanal (III).

The ultraviolet absorption spectrum of 2,2,4-triphenyl-3-butenal (III) (Fig. 1) shows two absorption bands at λ 2500 A (log ε 3.3) and λ 3100 A (log ε 2.4), characteristic for the styryl and carbonyl group, respectively [1, 3].

When the same glycol was heated with 30% aqueous H_2SO_4 solution, we again isolated 2,2,4-triphenyl-3-butenal (III) (50%) and, in addition, a crystalline product (15%) with the empirical formula $C_{22}H_{18}O$, to which we assigned the formula 2,3,5-triphenyl-2,5-dihydrofuran (V). The ultraviolet absorption spectrum of 2,3,4-triphenyl-2,5-dihydrofuran (V) (Fig. 1) shows only one absorption maximum at λ 2500 A (log ε 3.2), caused by conjugation of the phenyl group with the double bond. It was shown by É. D. Venus-Danilova and A. Fabritsy [4] that the absorption curve for 5,5-dimethyl-2,4-diphenyl-2-hydroxy-2,5-dihydrofuran is also characterized by having only one maximum at λ 2520 A.

In the table we give the infrared-absorption values for compound (V), which characterize this compound as being a 2,5-dihydrofuran. The absorption band with a wave number of 1080 cm^{-1} is a characteristic frequency for the valence vibration of C-O in C-O-C [5, 6]. Furan, and compounds related to it, absorb in the interval 1100-1075 cm^{-1} [6].

2,3-Dimethyl-5-phenyl-4-pentene-2,3-diol (II), new in the literature, was synthesized by the hydrogenation of the corresponding acetylenic glycol [7] in the presence of colloidal palladium. Here two geometric (cis, trans) isomers of this ethylenic glycol were isolated.

It is indicated in the literature [14] that an analysis of the infrared and ultraviolet absorption spectra could be of assistance in deciding as to the geometric configuration of a compound. The empirical rule is known that that the trans-isomer absorbs more intensely in the ultraviolet than does the cis-isomer. The absorption curves for the cis- and trans-isomers of 2,3-dimethyl-5-phenyl-4-penetene-2,3-diol (II) are shown in Fig. 2, while in the table we have given their infrared spectra, where the frequency 950 cm^{-1} corresponds to the trans-position of $-CH=CH-$ in the glycol group. Both isomers of the ethylenic and of the original acetylenic glycol gave the

Infrared Absorption Spectra* (wave numbers, cm^{-1})

2,3,5,- Triphenyl-2,5-dihydrofuran (V)	2,3-Dimethyl-5-phenyl-4-penture-2,3-diol (II)		4,5,5,-Trimethyl-2-phenyl-2,5-dihydrofuran (VI)
	cis-isomer	trans-isomer	
	848 (s.)	846 (av.)	
926 (av.)	899 (av.)	893 (av.)	697 (s.)
		950 (v.s.)	
949 (av.)	986 (v. w.)	986 (v. w.)	758 (s.)
1020 (v. s.)	1027 (w.)	1027 (w.)	849 (w.)
1037 (v. s.)	1064 (v. s.)	1064 (v. s.)	842 (av.)
1080 (v.s.)	1084 (v. s.)	1088 (v. s.)	965 (av.)
1189 (av.)	1125 (v. s.)	1123 (v. s.)	1052 (v. s.)
1229 (s.)	1152 (v. s.)	1150 (v. s.)	1130 (v. s.)
1295 (s.)	1177 (w.)	1178 (v. s.)	1167 (av.)
1300 (w.)	1263 (s.)	1264 (w.)	1178 (av.)
1350 (w.)	1344 (v. s.)	1338 (s.)	1441 (v. s.)
1529 (s.)	1368 (av.)	1368 (v. s.)	1490 (av.)
1597 (av.)	4443 (av.)	1448 (s.)	1605 (s.)
1615 (s.)	1478 (av.)	1493 (s.)	1661 (av.)
1810 (s.)	1573 (w.)	1573 (w.)	
	1602 (s.)	1600 (s.)	
		1635 (v. w.)	

*s. – bands with strong intensity, v.s. – bands with very strong intensity, med. – bands with medium intensity, w. – bands with weak intensity.

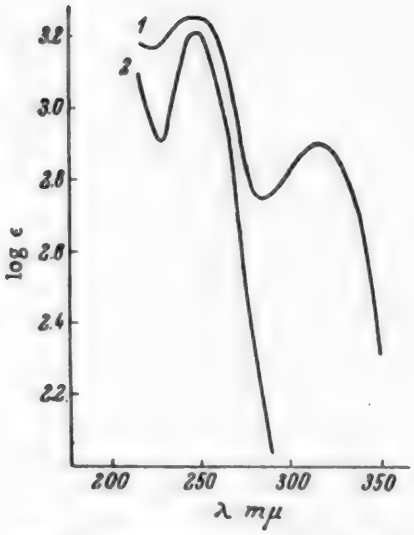


Fig. 1. Ultraviolet spectra. 1) 2,2,4-triphenyl-3-butenal (III), 2) 2,3,5-triphenyl-2,5-dihydrofuran (V).

The treatment of 2,3-dimethyl-5-phenyl-4-pentene-2,3-diol (II) with 20 alcoholic H_2SO_4 solution at 50°, and with 30% aqueous H_2SO_4 solution at 90-100°, gave but a single substance with the empirical formula $C_{13}H_{16}O$, to which, on the basis of its properties, we believe it possible to assign the structure of 4,5,5-trimethyl-2-phenyl-2,5-dihydrofuran (VI).

To support the proposed structure, we took both its ultraviolet and infrared absorption spectra.

The ultraviolet absorption spectrum of 4,5,5-trimethyl-2-phenyl-2,5-dihydrofuran is shown in Fig. 2 (curve 3), where it is compared with the absorption spectrum of the original glycol. In the investigated region of 2000-4000 A, the absorption curve for dihydrofuran (VI) (curve 3) has neither maxima nor minima, whereas the absorption curve for the original glycol has one intense absorption band at λ 2500 A (log ε 3.88). If, as mentioned above, it is assumed that in our case the appearance of an absorption band at λ 2500 A is due to the presence of the styryl group in the molecule, then it is possible to conclude that conjugation of the double bond with the benzene ring is absent in the investigated isomerization product of 2,3-dimethyl-5-phenyl-4-pentene-2,3-diol.

The ultraviolet absorption spectrum is given in the table, and does not require a detailed interpretation. In the main, it is comparable to the absorption spectrum of 2,4,5-triphenyl-2,5-dihydrofuran.

Scheme 1 shows the transformation of 1,2,4-triphenyl-3-butene-1,2-diol (I) and of 2,3-dimethyl-5-phenyl-4-pentene-2,3-diol (II).

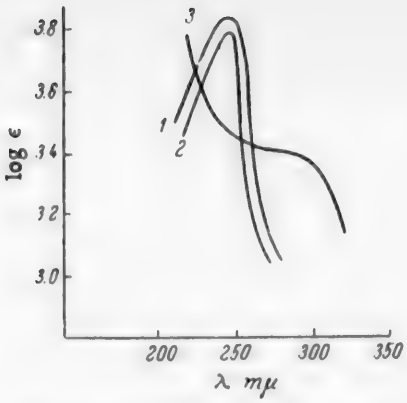
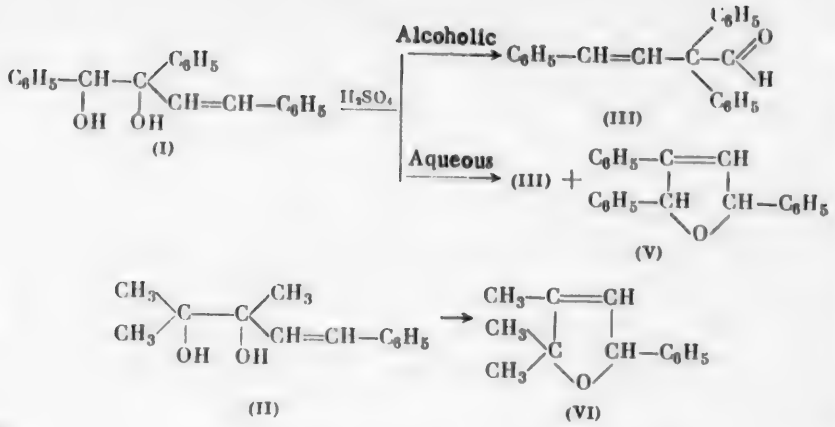


Fig. 2. Ultraviolet spectra. 1) 2,3-Dimethyl-5-phenyl-4-pentene-2,3-diol (trans), 2) 2,3-dimethyl-5-phenyl-4-pentene-2,3-diol (cis), 3) 4,5,5-trimethyl-2-phenyl-2,5-dihydrofuran(VI).

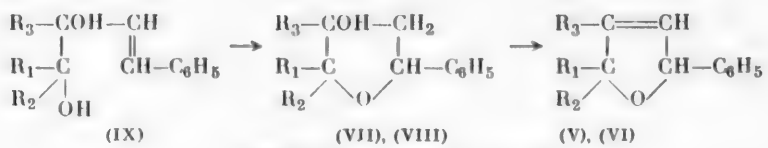
Scheme 1



Aldehyde (III) is formed as the result of the pinacolin rearrangement of glycol (I), while the substituted 2,5-dihydrofurans (V) and (VI), the same as in the case of 2-methyl-3,5-diphenyl-4-pentene-2,3-diol [3], are formed via the allylic rearrangement of the starting glycols, with the intermediate formation of the ethylenic γ-glycol $R_1R_2COH - C(R_3)=CH - CHOH - C_6H_5$ (IV), the subsequent dehydration of which leads to closure of the dihydrofuran ring.

It should be mentioned that the ethylenic α-glycols (IX) can also isomerize to the substituted dihydrofuran by a different route (scheme 2), which is all the more probable, since we were unable to isolate the intermediate γ-glycol (IV).

Scheme 2



(V) & (VII) $R_1 = H$; $R_2 = R_3 = C_6H_5$,
(VI) & (VIII) $R_1 = R_2 = R_3 = CH_3$.

In this case cyclization first occurs through the double bond and the hydroxyl, standing β to it, with the formation of β-tetrahydrofuranol (VII) or (VIII); the latter on dehydration give dihydrofurans (V) or (VI). Such a reaction course is confirmed to some degree by the studies of T. A. Favorskaya and co-workers[8-11], who established that the formation of substituted tetrahydrofurans in the dehydration of certain γ-glycols can occur, not by the liberation of water with involvement of the two hydroxyls of the glycol, but via the formation of the unsaturated β-ethylenic alcohol, which then isomerizes to the tetrahydrofuran under the dehydration conditions prevailing in the acid medium.

EXPERIMENTAL

Transformation of 1,2,4-Triphenyl-3-butene-1,2-diol (I)

Expt. I. Action of alcoholic H_2SO_4 solution. Into a flask, fitted with mechanical stirrer, was charged 20 g of the ethylenic glycol with m.p. 122-123° [12], 120 ml of 96% alcohol and 10.6 ml of sulfuric acid (d 1.84), and the mixture heated on the water bath at 60-70° for 4 hours. Within 30 minutes the solution had assumed a yellow color. At the end of heating, the solution was poured into 200 ml of cold water; the acid solution was extracted with ether. The ether extract was washed with water, then with sodium carbonate solution, again with water, and finally it was dried over sodium sulfate. Removal of the ether by distillation left a dark-red oily liquid,

which on standing deposited 3 g of crystals, the melting point of which was the same as that of the original glycol (mixed melting point). The crystals were filtered, while the liquid was vacuum-distilled. The yield of product, a light-yellow viscous liquid, was 80%, based on starting glycol. The substance showed the absence of hydroxyl when tested with Grignard reagent, the presence of the carbonyl group when tested with 2,4-dinitrophenylhydrazine, decolorized both aqueous potassium permanganate solution and bromine water, and, as was shown by oxidation, corresponded to 2,3,4-triphenyl-3-butenal (III), new in the literature.

B.p. 210-212° (1 mm), d_4^{20} 1.1320, $n^{20}D$ 1.6370, MR_D 94.16. $C_{22}H_{18}O$F. Calculated 92.54.

Found %: C 88.28; H 6.00. M 300. $C_{22}H_{18}O$. Calculated %: C 88.56; H 6.04. M 298.

When the substance with b.p. 210-212° (1 mm) was reacted with 2,4-dinitrophenylhydrazine, we obtained the 2,4-dinitrophenylhydrazone with m.p. 76-78°.

Found %: N 12.00, 11.70. $C_{28}H_{22}O_4N_4$. Calculated %: N 11.73.

To determine its structure, 4 g of the substance with b.p. 210-212° (1 mm) was oxidized in the cold. In the course of 3 days we added 100 ml of 5% $KMnO_4$ solution in drops, and on the fourth day we added another 1 g of dry $KMnO_4$ in small portions. The manganese dioxide was filtered. Neutral products were not found among the oxidation products. The salts of the acids were evaporated partially. Acidification resulted in the deposition of colorless crystals. The benzoic acid was removed by sublimation, and had m.p. 120-121° (mixed melting point).

The crystals remaining after removal of the benzoic acid were subjected to steam distillation. The third fraction of the distillate gave an acid with m.p. 143-145° [13], corresponding to diphenylacetic acid. The mixed melting point with an authentic specimen of diphenylacetic acid was not depressed. The silver salt was prepared, and its analysis for silver gave a satisfactory result.

Expt. II. Action of 30% aqueous H_2SO_4 solution. With mechanical stirring, a mixture of 10 g of the ethylenic glycol (m.p. 122-123°) and 150 ml of 30% aqueous sulfuric acid solution was heated on the water bath at 60-80°. Within 15 minutes after the start of heating the glycol liquefied, and the liquid assumed a yellow-green color. After 4 hours the solution was poured into 250 ml of water, and then extracted with ether. The ether extract was washed with water, then with 10% sodium carbonate solution, again with water, and finally it was dried over sodium sulfate. Removal of the ether by distillation left a mixture of oily liquid and crystalline substance. The liquid was filtered from the crystals, and then vacuum-distilled. The distillation gave a light-yellow oily substance.

B.p. 212-213° (1 mm), d_4^{20} 1.1324, $n^{20}D$ 1.6367, MR_D 94.16. $C_{22}H_{18}O$F. Calculated 92.54.

Found %: C 88.16; H 6.60. M 304. $C_{22}H_{18}O$. Calculated %: C 88.56; H 6.04. M 298.

The 2,4-dinitrophenylhydrazone had m.p. 76-78°.

Found %: N 12.40. $C_{28}H_{22}O_4N_4$. Calculated %: N 11.73.

Consequently, the liquid substance was the unsaturated aldehyde, obtained and characterized in the preceding experiment.

The crystals, separated from the aldehyde, were recrystallized twice from alcohol. Very rapidly, there first deposited 2 g of a colorless crystalline substance with m.p. 121-122°, which failed to depress the melting point when mixed with the starting ethylenic glycol.

After 3 days the mother liquor deposited 2.5 g of colorless crystals, which, after recrystallization from alcohol, had m.p. 78-79°. A second recrystallization gave the same result. The substance rapidly turns yellow in the air, gives a sky blue color with conc. sulfuric acid, and decolorizes both bromine water and aqueous potassium permanganate solution with difficulty. The reaction for hydroxyl with Grignard reagent, and for carbonyl group with 2,4-dinitrophenylhydrazine, were negative. From the analysis data and its properties, the substance can be assumed to be 2,3,5-triphenyl-2,5-dihydrofuran (V), not described in the literature.

Found %: C 89.36; H 5.94. M 299. $C_{22}H_{18}O$. Calculated %: C 88.59; H 6.00. M 298.

Synthesis of 2,3-Dimethyl-5-phenyl-4-pentene-2,3-diol (II)

2,3-Dimethyl-5-phenyl-4-pentene-2,3-diol was obtained by the hydrogenation of trimethyl(phenylethynyl) ethylene glycol [7] in the presence of colloidal palladium. A solution of 22.4 g of the acetylenic glycol (b.p. 150-152° at 5 mm) in 100 ml of alcohol was hydrogenated in the presence of 3 mg of colloidal palladium. In 30 minutes, after the absorption of 2700 ml of hydrogen (18°, 755 mm), the hydrogenation was stopped, the catalyst was filtered, and the alcohol was removed by distillation. The residual light-yellow viscous liquid was vacuum-distilled, and here two substances were isolated: one with b.p. 137-138° (3 mm), and the second with b.p. 141-143° (3 mm).

Based on the analysis data, both substanceshave the same composition and molecular weight. Hydrogenation of these substances in the presence of platinum black gave the same saturated glycol with m.p. 68-70°. On the basis of these data, and the infrared and ultraviolet absorption spectra (see table), it can be assumed that the substances with b.p. 137-138° (3 mm) and 141-143° (3 mm) are geometric isomers. The substance with b.p. 137-138° (3 mm) corresponds to the trans-isomer, and that with b.p. 141-143° (3 mm), to the cis-isomer.

Investigation of the trans-Isomer with b.p. 137-138° (3 mm):

$n^{20}D$ 1.5432, d_4^{20} 1.050, MR_D 61.80. $C_{13}H_{18}O_2F$. Calculated 61.22.

Found %: C 75.48; H 8.75; OH 16.40. M 202. $C_{13}H_{18}O_2$. Calculated %: C 75.52; H 8.73; OH 16.50. M 206.

The hydrogenation of 1.8 g of the trans-isomer in 15 ml of alcohol in the presence of 0.2 g of platinum black until saturation required 18 minutes and resulted in the absorption of 230 ml of hydrogen (18°, 760 mm). After removal of the catalyst and alcohol, the residual viscous liquid crystallized; 3 recrystallizations from petroleum ether gave 1.2 g of colorless crystals with m.p. 68-70°, being the previously unknown 2,3-dimethyl-5-phenyl-2,3-pentanediol.

Found %: C 75.45; H 9.65; OH 16.34. M 203. $C_{13}H_{20}O_2$. Calculated %: C 75.00; H 9.70; OH 16.00. M 208.

The saturated glycol, described for the first time, gives a pale yellow color with conc. H_2SO_4, and does not decolorize either bromine water or potassium permanganate solution.

Investigation of the cis -Isomer With b.p. 141-153° (3 mm):

$n^{20}D$ 1.5425, d_4^{20} 1.055, MR_D 61.5; calc. 61.21.

Found %: C 75.50; H 8.70; OH 16.01. M 200. $C_{13}H_{18}O_2$. Calculated %: C 75.52; H 8.73; OH 16.50. M 206.

The addition of 2 atoms of hydrogen resulted in the isolation of crystals with m.p. 68-70°, which failed to depress the melting point when mixed with the substance obtained in the hydrogenation of the trans-isomer. The cis-isomer adds hydrogen twice as fast as the trans-isomer. The amount of substance taken and the hydrogenation conditions for the cis-isomer were exactly the same as for the case of the trans-isomer.

Transformation of 2,3-Dimethyl-5-phenyl-4-pentene-2,3-diol (II)

Expt. I. Action of alcoholic H_2SO_4 solution. Into a flask, fitted with mechanical stirrer, was charged 8.5 g of the cis-isomer of the ethylenic glycol (b.p. 141-143° at 3 mm), 50 ml of 96% ethyl alcohol and 5.3 ml of sulfuric acid (d 1.84). The mixture assumed a yellow color immediately. After heating for 3 hours at 50°, the solution was poured into cold water, and then extracted with ether. The ether was distilled off, while fractional distillation of the residue gave 6.4 g (77%) of a nearly colorless mobile liquid, which rapidly turned dark in the air, showed the absence of both hydroxyl and the carbonyl group, and decolorized both aqueous potassium permanganate solution and bromine water. Based on the analysis data, the obtained substance can be assumed to be 4,5,5-trimethyl-2-phenyl-2,5-dihydrofuran (VI).

B.p. 108-110° (5 mm), $n^{20}D$ 1.522, d_4^{20} 0.9740, MR_D 58.74. $C_{13}H_{16}OF$. Calculated 57.60.

Found %: C 83.55; H 8.42. M 186.9. $C_{13}H_{16}O$. Calculated %: C 83.00; H 8.41. M 188.

The substance is not described in the literature. It gives a blue violet fluorescence with conc. H_2SO_4.

Expt. II. Action of 30% aqueous H_2SO_4 solution. A mixture of 10 g of the ethylenic glycol with b.p. 141-143° (3 mm) and 30% aqueous H_2SO_4 solution was heated in a flask, with mechanical stirring, at 90-100° for 2.5 hours. At the end of heating, the mixture was poured into water, and then worked up as indicated in the preceding experiment. Fractional distillation in vacuo gave 7.5 g of substance with b.p. 107-109° (5 mm), which in its physical properties was identical with 4,5,5-trimethyl-2-phenyl-2,5-dihydrofuran.

Taking of the Absorption Spectra. The ultraviolet absorption spectra* were taken with a SF-4 quartz photoelectrospectrophotometer, while a GOI hydrogen lamp served as the light source. Alcohol was used as the solvent; the solutions used for taking the spectra ranged in concentration from 0.01 to 0.0005 mole/ml.

The infrared-absorption spectra were photographed using IKS-2 and IKS-14 spectrophotometers, NaCl prisms, and LiCl cuvettes, while the layer thickness was 0.5 to 0.001 mm. Compounds (V) and (VI) were photographed in CCl_4 solution.

SUMMARY

1. It was shown that when treated with 20% alcoholic H_2SO_4 solution of 1,2,4-triphenyl-3-butene-1,2-diol is converted to 2,2,4-triphenyl-3-butenal, and when treated with 30% aqueous H_2SO_4 solution, it is converted to 2,2,4-triphenyl-3-butenal and 2,3,5-triphenyl-2,5-dihydrofuran.

2. Both the cis- and trans-isomers of 2,3-dimethyl-5-phenyl-4-pentene-2,3-diol were synthesized. It was shown that treatment of the cis-isomer with either 20% alcoholic or 30% aqueous H_2SO_4 solution results in its transformation to 4,5,5-trimethyl-2-phenyl-2,5-dihydrofuran.

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PREPARATION AND ISOMERIZATION OF MIXED ESTERS OF DI-(1,3-DICHLOROISOPROPYL)PHOSPHOROUS ACID. V

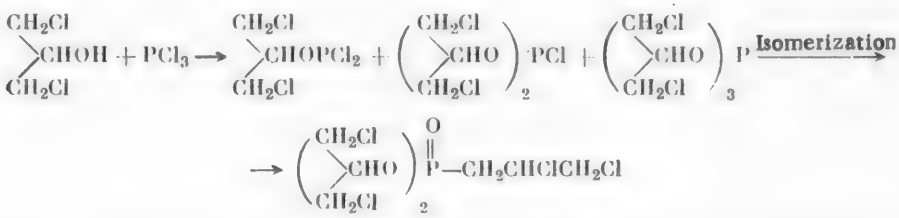
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Earlier we studied the reactions of acid chlorides corresponding to mono- and di-tert-(trichloromethyl) alkylphosphorous acids with various alcohols in the presence of an organic base [1], as a result of which the corresponding mixed phosphorous acid esters were obtained. The good yields of the mixed esters show that they are stable on distillation, and disproportionation of the ester radicals is not observed. It is of interest to prepare mixed phosphorous acid esters with other halogen-containing ester radicals and to study the effect of halogens on their properties.

Depending on the nature of the radical, the presence of substituents therein, and the reaction conditions, alcohols react with phosphorus trichloride to form alkoxydichlorophosphines, dialkoxychlorophosphines, dialkylphosphorous acids, and trialkyl phosphites. Chlorosubstituted [2] and cyano-substituted [3] alcohols react with phosphorus trichloride to give alkoxychlorophosphines and, in some cases, phosphites.

1,3-Dichloropropanol-2, which we chose as the subject of investigation, reacts with phosphorus trichloride at room temperature and gives the following products: (1,3-dichloroisopropoxy)dichlorophosphine in 22% yield, di-(1,3-dichloroisopropoxy)chlorophosphine in 25.4% yield, and di(1,3-dichloroisopropyl) (2,3-dichloropropyl) phosphonate in 9.8% yield; the latter evidently is obtained as a result of intra- or intermolecular isomerization of the tri-(1,3-dichloroisopropyl) phosphite formed in the course of the reaction, according to the scheme studied and proposed some time ago by M. I. Kabachnik and P. A. Rossiiskaya [4]. Isomerization probably takes place both during the reaction and on fractionation of the reaction products. The reaction of 1,3-dichloropropanol-2 with phosphorus trichloride may be represented by the scheme



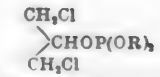
The full ester of phosphorous acid was not isolated in pure form; however, the intermediate fraction preceding the isomerized ester reacts with cuprous chloride with evolution of heat [5], which may be used to indicate the presence of a phosphite.

Di(1,3-dichloroisopropoxy)chlorophosphine, on treatment with water, was converted to the corresponding phosphorous acid, which was then condensed with aldehydes and ketones.

(1,3-Dichloroisopropoxy)dichlorophosphine was used for the synthesis of mixed phosphorous acid esters, which were obtained through reaction with aliphatic alcohols in the presence of pyridine in an absolute ether medium at (-6)-0°. The yield of esters amounted to 47-65%. On fractionation of the reaction products low-

TABLE 1

Physical Properties of Mixed Phosphorous Acid Esters

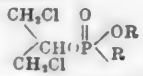


No.	R	Boiling point (pressure in mm)	d_4^{20}	n_D^{20}	MR_D found	MR_D calculated	Yield (in %)	% Cl* found	% Cl* calculated	% P* found	% P* calculated
1	CH_3	84° (4)	1.2875	1.4680	48.00	48.13	47.5	32.12	32.08	13.83	14.02
2	C_2H_5	84— 86 (1.5)	1.1890	1.4605	57.43	57.35	65.0	28.51	28.40	12.37	12.40
3	n-C_3H_7	105—107 (2)	1.1393	1.4585	66.48	66.60	51.0	25.34	25.60	10.98	11.18
4	n-C_4H_9	122—124 (1)	1.1990	1.4550	75.77	75.85	53.0	23.18	23.24	10.12	10.15

* Values of the chlorine and phosphorus content in the "found" column are averages of two determinations.

TABLE 2

Physical Properties of Alkyl-(1,3-dichloroisopropyl) Alkylphosphonates



No.	R	Boiling point (pressure in mm)	d_4^{20}	n_D^{20}	MR_D found	MR_D calculated	Yield (in %)	% Cl* found	% Cl* calculated	% P* found	% P* calculated
1	C_2H_5	100 (1)	1.2470	1.4610	55.00	55.13	50.0	28.12	26.40	12.23	12.40
2	n-C_4H_9	140—142 (1.5)	1.1326	1.4585	73.60	73.53	66.7	23.26	23.24	10.25	10.15

* Values of the chlorine and phosphorus content in the "found" column are averages of two determinations.

boiling fractions with extended boiling ranges, which reacted exothermically with cuprous chloride, were obtained in all cases. However, it was not possible to isolate definite substances. The picture observed on fractionation calls to mind the fractionation of mixed aliphatic phosphites [6]. From this we conclude that in the fractionation of the chlorine-containing mixed phosphites which we prepared, the ester radicals are disproportionated. The relatively low yields of mixed esters also indicate a disproportionation process. Mixed dialkyl-(1,3-dichloroisopropyl) phosphites are colorless, mobile liquids with a slight odor, similar to that of triethyl phosphite. They all react exothermically with cuprous chloride and give complex compounds in the form of thick, noncrystallizing sirups. The physical properties of the mixed esters obtained are given in Table 1.

Two of the mixed phosphites obtained were isomerized by treatment with the corresponding alkyl iodides. The reaction of isomerization with an alkyl iodide and splitting-off of an unsubstituted aliphatic radical goes smoothly [7]. The rate of reaction of the ester radical with alkyl chlorides is evidently negligible, and therefore no intra- or intermolecular isomerization products are found. The physical properties of the isomerization products of mixed phosphites are given in Table 2.

On treatment of (1,3-dichloroisopropoxy)dichlorophosphine in ethereal solution with water, the corresponding acid is obtained in the form of a viscous, oily liquid. The resulting acid and alkyl-(1,3-dichloroisopropyl) alkylphosphonates (Table 2) were used for reactions of condensation with calcium polysulfide. The condensation was carried out by the generally used method [8] it proceeded at room temperature. Condensation products were obtained in the form of yellowish powders, insoluble in common organic solvents.

EXPERIMENTAL

Reaction of 1,3-Dichloropropanol-2 with Phosphorus Trichloride. A 274.7 g quantity of phosphorus trichloride was placed in a three-neck liter flask provided with dropping funnel, thermometer, mechanical stirrer, and reflux condenser closed with a calcium chloride tube. The hydrogen chloride evolved was absorbed by water. Then 258 g of anhydrous 1,3-dichloropropanol-2 was added dropwise during 3 hours at room temperature with vigorous stirring. After the addition, stirring was continued for 1.5 hours more. The hydrogen chloride was drawn off in vacuo. On fractionation of the reaction products the following fractions were isolated: 1st – up to 100° (15-12 mm), 16 g; 2nd – 100-115° (12 mm), 111 g; 3rd – 115-139° (2 mm), 123 g; 4th – 139-208° (2 mm), 63 g; 5th – 208-210° (2 mm), 31 g; residue 9 g.

On redistillation of the second fraction there was obtained 100.2 g (22%) of (1,3-dichloroisopropoxy)dichlorophosphine.

B.p. 75° (2 mm), d_4^{20} 1.4973, $n^{20}D$ 1.5195, MR_D 46.73. $C_3H_5OCl_4P$. Calculated 46.10.

From the third fraction 99.3 g (25.4%) of di-(1,3-dichloroisopropoxy) chlorophosphine was obtained.

B.p. 135-137° (1 mm), d_4^{20} 1.4903, $n^{20}D$ 1.5189, MR_D 65.66. $C_6H_{10}O_2Cl_5P$. Calculated 66.09.

The fraction amounting to 31.3 g (9.8%) consisted of di-(1,3-dichloroisopropyl) (2,3-dichloropropyl)phosphonate.

B.p. 208-210° (2 mm), d_4^{20} 1.5018, $n^{20}D$ 1.5130, MR_D 83.38. $C_9H_{15}O_3Cl_6P$. Calculated 83.32.

The fourth (crude) fraction reacted with cuprous chloride with evolution of heat. Repeated distillation for the purpose of isolating the phosphite was unsuccessful.

Preparation of Dibutyl-(1,3-dichloroisopropyl)phosphite. A 25.8 g quantity of butanol-1 and 27.5 g of pyridine in 250 ml of anhydrous ether were placed in a 500 ml, three-neck flask, equipped as described above. Forty g of (1,3-dichloroisopropoxy)dichlorophosphine was added dropwise at such a rate that the temperature did not exceed 0°, the mixture being cooled with ice and salt and stirred. Stirring was then continued at room temperature for 30 minutes and during refluxing for 30 minutes. On cooling, the pyridine hydrochloride was filtered out, the ether driven off, and the residue distilled in vacuo. After two successive fractionations the following fractions were isolated: 1st – up to 122° (1 mm), 5.7 g; 2nd – 122-124° (1 mm), 31.1 g; residue 6.5 g.

The fraction with b.p. 122-124° (1 mm) was dibutyl-(1,3-dichloroisopropyl)phosphite, the constants and analyses of which are given in Table 1.

The preparation of other mixed phosphorous acid esters was similar.

When a mixture of 14.0 g of methanol and 50 g of (1,3-dichloroisopropoxy)dichlorophosphine was distilled twice, there were obtained the fractions: 1st – up to 87° (4 mm), 7 g; 2nd – 87° (4 mm), 22.3 g; residue 4 g.

From 27.5 g of alcohol and 40 g of (1,3-dichloroisopropoxy)dichlorophosphine were obtained the fractions: 1st – up to 84° (1.5 mm), 4 g; 2nd – 84-86° (1.5 mm), 29 g; residue 4.5 g.

From 10.6 g of propanol-1 and 20 g of (1,3-dichloroisopropoxy)dichlorophosphine were obtained the fractions: 1st – up to 105° (2 mm), 2 g; 2nd – 105-107° (2 mm), 12.3 g; residue 3 g.

The middle fractions were dialkyl-(1,3-dichloroisopropyl)phosphites. Their constants and analyses are given in Table 1.

Isomerization of Diethyl-(1,3-dichloroisopropyl) Phosphite With Ethyl Iodide. Six g of ethyl iodide and 26 g of diethyl-(1,3-dichloroisopropyl) phosphite were sealed in an ampule. After the ampule was heated in a boiling-water bath for 15 hours, it was opened, the ethyl iodide distilled off (5 g), and the residue fractionated in vacuo. There was isolated 13 g (50%) of ethyl-(1,3-dichloroisopropyl) ethylphosphonate.

B.p. 100° (1 mm), d_4^{20} 1.2470, $n^{20}D$ 1.4610 MR_D 55.00 $C_7H_{15}O_3Cl_2P$. Calculated 55.13.

Isomerization of Dibutyl-(1,3-dichloroisopropyl) Phosphite with Butyl Iodide. An ampule containing 29.5 g of the dibutyl-(1,3-dichloroisopropyl) ester and 5 g of butyl iodide was heated at 100° for 16 hours. From the reaction products 19.7 g (66.7%) of butyl-(1,3-dichloroisopropyl) butylphosphonate was obtained.

B.p. 140-142 (1.5 mm), d_4^{20} 1.1326, $n^{20}D$ 1.4585, MR_D 73.60. $C_{11}H_{23}O_3Cl_2P$. Calculated 73.53.

Preparation of (1,3-dichloroisopropyl)phosphorous Acid. A 98.85 g quantity of (1,3-dichloroisopropoxy) dichlorophosphine and 100 ml of ether were put into a three-neck flask provided with dropping funnel, thermometer, mechanical stirrer, and gas outlet tube. The flask was kept cold with ice and salt, and 15.5 ml of water was added dropwise at such a rate that the temperature in the flask did not exceed 0°. The reaction products stood for 30 minutes at room temperature, after which hydrogen chloride and ether were removed in vacuo by heating to 100°, the residue was a viscous, oily liquid which, according to its constants and analysis, consisted of (1,3-dichloroisopropyl)phosphorous acid.

d_4^{20} 1.5040, $n^{20}D$ 1.4860, MR_D 36.82. Calculated 36.54.

Found %: Cl 36.88, 36.96; P 15.75, 15.61. $C_3H_7O_3Cl_2P$. Calculated %: Cl 36.74; P 16.05.

SUMMARY

1. A study has been made, of the reaction between 1,3-dichloropropanol-2 and phosphorus trichloride, which leads to the formation of: (1,3-dichloroisopropoxy)dichlorophosphine, di(1,3-dichloroisopropoxy)-chlorophosphine, and di-(1,3-dichloroisopropyl) (2,3-dichloropropyl)phosphonate, the latter being obtained through isomerization of tri-(1,3-dichloroisopropyl) phosphite.

2. Mixed dialkyl-(1,3-dichloroisopropyl) phosphites have been synthesized.

3. Isomerization of the mixed phosphites by the corresponding alkyl iodide goes smoothly, with splitting-off of the unsubstituted aliphatic alkyl radical and formation of alkyl-(1,3-dichloroisopropyl) alkylphosphonates.

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USE OF N,N'-DICYCLOHEXYLCARBODIIMIDE FOR THE SYNTHESIS OF OXAZOLIN-5-ONES SUBSTITUTED IN POSITIONS 2 AND 4

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In recent years carbodiimides have found wide application in organic synthesis. After the publication of a monograph on the chemistry of carbodiimides [1], in which methods of their preparation and also their physical and chemical properties were described, a number of papers on new ways of using them appeared in the literature. N,N'-Dicyclohexylcarbodiimide became especially important [2-5] as one of the compounds that are accessible and convenient in use.

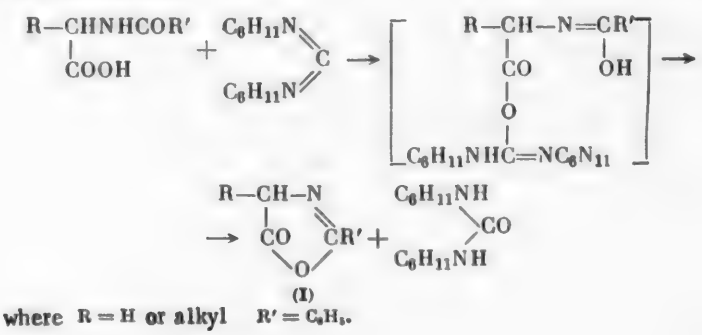
N,N'-Dicyclohexylcarbodiimide was used in the synthesis of peptides [6,7], carboxylic acid esters [8], alkyl- and arylsulfonic acid anhydrides [9], pyrophosphoric acid esters from acid esters of phosphoric acid [10], and also adenosinedi-and -triphosphoric acids [11], P^1,P^2-diadenosine-5'-pyrophosphoric acid [11], and monoesters of ribonucleoside-2'- and 3'-phosphoric acids [12]. Besides, the reactions of N,N'-dicyclohexylcarbodiimide with alcohols [13], acid anhydrides [14], and cyanamide [15] were described. Finally, N,N'-dicyclohexylcarbodiimide was used for the synthesis of penicillin V from monopotassium phenoxymethylpenicilloate [16] and that of a series of other penicillins [17], and also isoreserpic acid lactone [24].

In the study of the reaction between N-acyl-a-amino acids and N,N'-dicyclohexylcarbodiimide in a dry chloroform medium it was established that oxazolin-5-ones substituted in position 2 or positions 2 and 4 are easily formed in this case. Thus, for instance, a-benzoylamino-β-chloroacrylic acid is very easily converted to 2-phenyl-4-(chloromethylen)-oxazolin-5-one, identified with that already described in the literature [18], the diethylacetal of formylhippuric acid gives the well-known 2-phenyl-4-(ethoxymethylen)oxazolin-5-one, which which was obtained earlier by heating hippuric acid with orthoformic ester and acetic anhydride [19], and hippuric acid forms 2-phenyloxazolin-5-one. The latter is easily prepared by heating hippuric acid with acetic anhydride [20-22].

The reaction between hippuric acid and N,N'-dicyclohexylcarbodiimides does not proceed as smoothly as the two preceding ones, and the reaction mass must be heated.

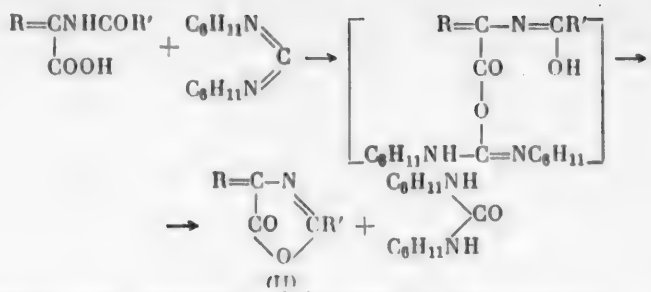
The reaction of formation of oxazolin-5-ones may be represented in the following general form:

a) For saturated oxazolin-5-ones:



where R = H or alkyl $R' = C_6H_5$.

b) For unsaturated oxazolin-5-ones:



where R = CH_3, CH_3CH etc., and also ClCH, C_2H_5OCH; R' = C_6H_5.

A special case of the Type "b" reaction is the conversion of the diethylacetal of formylhippuric acid to 2-phenyl-4-(ethoxymethylen)oxazolin-5-one (II, R = C_2H_5OCH; R' = C_6H_5), in which an alcohol molecule is split off.

In one of the papers it was shown that the reaction between N-acylamino acids and amino-acid esters in the presence of N,N'-dicyclohexylcarbodiimide leads to compounds with a peptide linkage, N-acyl-N,N'-dicyclohexylcarbamides being formed at the same time. The reaction proceeds by addition of the acylamino acid to one of the double bonds of the carbodiimide [6].

In the given case the intermediate compound (in square brackets) is shown as the tautomeric form of the amide. In the absence of an amino-acid ester it may undergo rearrangement either to an N-acyl-N,N'-dicyclohexylcarbamide or to oxazolin-5-one (I) or (II). Obviously the second reaction takes place much more readily than the first; this may be explained by the weakening of the bond between carbonyl and oxygen in the intermediate compound and the mobility of the hydrogen atom in the hydroxyl group. This is possibly facilitated by the steric arrangement of the groups which form the azlactone ring.

N,N'-Dicyclohexylcarbodiimide, being a more expensive substance than ordinary azlactonizing compounds, can be recommended only in special cases. Its advantage consists in the fact that it separates from the reaction mass in the form of the difficultly soluble N,N'-dicyclohexylcarbamide, which facilitates the work of isolating the oxazolin-5-ones in pure form. Besides, the conversion of N-acyl-α-amino acids to oxazolin-5-ones by means of this carbodiimide takes place even at room temperature in a number of cases without requiring preliminary heating; this is of substantial importance.

EXPERIMENTAL

2-Phenyl-4-(chloromethylenoxazolin-5-one. One g of α-benzoylamino-β-chloroacrylic acid was added to a solution of 1 g of N,N'-dicyclohexylcarbodiimide in 10 ml of dry chloroform. Heat was evolved, and N,N'-dicyclohexylcarbamide was immediately precipitated. On the next day the precipitate was filtered out and washed with chloroform. Weight 1 g. M.p. 224-226°. The chloroform was removed from the filtrate at room temperature; in this case a residue of light-green crystals was obtained, which was treated with 5 ml of absolute alcohol. Yield 0.9 g. After recrystallization from absolute alcohol fine, pale-yellow needles with m.p. 126.5-127.5° were obtained. Yield 0.75 g (81.5%).

Found %: C 57.83, 57.55; H 2.98, 2.91; N 6.54, 6.56; Cl 17.00. $C_{10}H_6O_2NCl$. Calculated %: C 57.83; H 2.91; N 6.74; Cl 17.03.

2-Phenyl-4-(ethoxymethylen)oxazolin-5-one. To a solution of 1.1 g of dicyclohexylcarbodiimide in 10 ml of dry chloroform was added 1.4 g of the diethylacetal of formylhippuric acid. The solid matter immediately dissolved, the solution warmed up slightly, and N,N'-dicyclohexylcarbamide precipitated. On the next day the latter was filtered out and washed with chloroform (1.1 g). The chloroform was removed at room temperature, and the crystalline residue was recrystallized from benzine, charcoal being used. Silky, pale-yellow needles with m.p. 96-97° were obtained. Yield 0.6 g (55.5%).

On reaction with alcoholic ammonia solution there was obtained 2-phenyl-4-(aminomethylen)-oxazolin-5-one, m.p. 213-215° (dec.); this is described in the literature [23].

Found %: C 66.41; H 5.06; N 6.46. $C_{12}H_{11}O_3N$. Calculated %: C 66.35; H 5.10; N 6.44.

2-Phenyloxazolin-5-one. To a solution of 2.2 g of N,N'-dicyclohexylcarbodiimide in 15 ml of dry chloroform was added 1.79 g of hippuric acid. The solid matter did not dissolve. On agitation the mass thickened and acquired a slight yellow tinge. On the next day it was refluxed in a water bath for 6 hours; in this case the character of the crystalline solid matter changed. On cooling, the precipitate of N,N'-dicyclohexylcarbamide was filtered out and washed with chloroform. Weight 2.1 g, m.p. 225-226°.

After evaporation of the chloroform the residue consisted of coarse, yellow tablets, which were recrystallized from anhydrous alcohol. M.p. 90-92°. Yield 0.9 g (56%).

Found %: C 66.82; H 4.56; N 8.64. $C_9H_7O_2N$. Calculated %: C 67.07; H 4.38; N 8.68.

SUMMARY

N,N'-Dicyclohexylcarbodiimide has been used for the synthesis of oxazolin-5-ones from hippuric and a-benzoylamino-β-chloroacrylic acids and the diethylacetal of formylhippuric acid.

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ON THE KINETICS OF THE MUTUAL CONVERSION OF CIS-TRANS ISOMERS

I. CARBOXYLIC ACIDS

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In the preceding article [1] we showed, for the case of a series of geometrically isomeric acids, that the cis-forms are always more easily reduced at the dropping-mercury cathode than the trans-forms; this is due to the greater content of free internal energy of the cis-modifications. From this we were justified in concluding that the introduction of photon energy from outside would promote the conversion of the trans-modifications to the cis-modifications, whereas exchange of this energy would cause the reverse transformation.

It should be noted that Stoermer, in a series of papers [2], long ago established the fact of the conversion of stable isomers to labile under the influence of ultraviolet light. Because of the difficulty of separating the isomers, however, he could not study the kinetics of the mutual conversions. We decided to follow the course of the conversion process, using the differences which we found [1] in the polarographic behavior of cis- and trans-isomeric acids.

Our attempts to isomerize the trans-forms of certain ethylenic acids, e.g., crotonic, fumaric, and aconitic, to the corresponding cis-forms by irradiation in the presence of suitable indifferent electrolytes (NH_4Cl or HCl) led to some unexpected results: the trans-modification usually disappeared gradually and the new form either did not appear at all or appeared in incongruously small quantity; the reverse transformation on standing in the dark did not occur. Assuming that in the given case some change takes place in the indifferent electrolyte under the influence of irradiation, we irradiated alcoholic solutions of hydrochloric acid and proved to our satisfaction that free chlorine appears in the solution in this case. Obviously this chlorine in statu nascendi adds to the double bonds of ethylenic compounds, causing irreversible transformations. To avoid this phenomenon, subsequent experiments on irradiation were performed in the absence of indifferent electrolytes.

EXPERIMENTAL

A solution of trans-cinnamic acid (0.01 M) and NH_4Cl (0.1 N) in 96% alcohol was irradiated with the light of a quartz-mercury lamp. From time to time two 5-ml samples were taken. One of them was diluted in a 10-ml pycnometer with alcoholic, and the other with aqueous 0.1 N ammonium chloride solution. Thus solutions of 5×10^{-3} M concentration were obtained, one in 96% alcohol and the other in 50% alcohol. The content of the trans-acid was determined polarographically in the first, and the total content of both acids in the second; from this the content of the cis-form could be calculated in particular. After 12-14 hours of irradiation the trans-isomer was quantitatively converted to the cis-isomer. At any particular instant the sum of the two forms was equal (within the limits of experimental error) to 5×10^{-3} M.

trans-Aconitic acid was irradiated in the form of a 0.01 M solution in 96% alcohol. Before being polarographed, the solution samples were diluted with twice their volume of 2 N aqueous hydrochloric acid; thus conditions were attained, under which the cis- and trans-acids gave clearly distinct waves on the polarization curve. Conversion of the trans-acid to the cis-acid was quantitatively complete after 5 hours.

Conversion of the cis-Modifications of Ethylenic Acids to the trans-Modifications

Acid	Time standing (days)	Conc. cis-isomer (mmol/liter)	Conc. trans-isomer (mmol/liter)	Total conc. isomers (mmol/liter)	K
Maleic, from irradiation of fumaric acid	0	5.17	—	5.17	—
	1	4.75	—	4.75	—
	3	4.54	—	4.54	0.043
	7	3.89	0.81	4.70	0.041
	9	3.46	1.43	4.89	0.045
	45	—	4.89	4.89	—
			Average		0.043
Maleic (C. P.), crystalline	0	5.00	—	5.00	—
	7	4.66	—	4.66	—
	9	3.33	1.57	4.90	0.045
	14	3.16	1.72	4.88	0.032
	28	1.16	3.92	5.08	0.052
	43	—	4.56	4.56	—
			Average		0.043
cis-Aconitic	0	5.18	—	5.18	—
	2	4.17	1.13	5.30	0.108
	4	3.60	1.40	5.00	0.091
	8	2.16	2.45	4.61	0.073
	50	—	4.90	4.90	—
			Average		0.091
Citraconic	0	4.94	—	4.94	—
	3	2.68	2.50	5.18	0.304
	5	2.07	3.54	5.61	0.174
	9	1.49	3.54	5.03	0.133
	20	—	5.00	5.00	—
			Average		0.170
Allocinnamic	0	5.00	—	5.00	—
	1	3.77	0.92	4.69	0.282
	2	3.59	1.41	5.00	0.166
	3	2.53	2.26	4.89	0.227
	4	1.10	4.09	5.19	0.379
	5	0.43	4.37	4.80	0.491
	6	—	4.80	4.80	—
			Average		0.309
Isocrotonic	0	9.95	—	9.95	—
	3	3.27	6.73	10.00	0.381
	5	0.84	8.88	9.72	0.495
	10	—	9.81	9.81	—
			Average		0.438

Mesaconic acid was irradiated in the form of a 6.67×10^{-3} M solution in 96% alcohol. In a 10-ml pycnometer, 7.5-ml samples were diluted to the mark with 4 N aqueous hydrochloric acid; thus a 5×10^{-3} M solution of the acid in 75% alcohol, containing 1 N hydrochloric acid, was obtained for polarographing; under these conditions mesaconic and citraconic acids gave two distinct waves on the polarization curve. Mesaconic acid was fully converted to citraconic after 6 hours of irradiation.

For irradiation of fumaric acid a 0.01 M solution of the latter in 96% alcohol was used. Five-ml samples were diluted for polarographing, with an equal volume of 0.2 N hydrochloric acid in 96% alcohol. Conversion of fumaric acid to maleic was complete after 5 hours of irradiation.

Crotonic acid was irradiated in the form of a 0.1 M solution in 96% alcohol. One-ml samples were taken two at a time; one of these was diluted in a 10 ml pycnometer to the mark with a 0.1 N solution of NH_4Cl in 96% alcohol, and the other was so diluted with 0.1 N aqueous NH_4Cl; the concentration of isocrotonic acid was determined in the first solution, and the total concentration of both isomeric acids in the second. The entire transition of crotonic acid to isocrotonic under the influence of irradiation was complete after 30 hours.

All the solutions of labile cis-acids, obtained by irradiation were left in the dark. Samples were periodically taken from these solutions and analyzed polarographically for their content of both geometric isomerics in order to follow the process of spontaneous conversion of the cis-modifications to the trans-modifications. The results found are given in the table. Reaction rate constants, calculated by means of the equation for the first-order reaction, are listed in the last column of this table. The figures obtained quite conclusively indicate the monomolecular character of the reaction, which, naturally, was to be expected.

The great stability of crystalline maleic acid is generally known. Apparently this stability is due to the fixed position of the molecules in the crystal and should vanish when the substance goes into solution. In order to test this hypothesis we prepared a solution of ordinary chemically pure, crystalline maleic acid and polarographically determined the composition of the solution after definite time intervals. The results of these analyses confirm our hypothesis.

Although the cis-forms of all ethylenic acids studied are labile, they differ greatly in the degree of their liability; maleic and cis-aconitic acids are much more stable than allocinnamic and isocrotonic.

SUMMARY

The kinetics of mutual conversion of the cis-trans-modifications of five ethylenic acids has been studied. A substantial diversity has been found in the degree of lability of the cis-modifications of different acids, which was determined from the rate constants of their conversion to the trans-modifications.

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SYNTHESIS OF α,β-DICHLOROPROPIONAMIDE

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Klimenko [1] and Beckurts and Otto [2] showed that in the reaction of ammonia with esters of halogen-substituted propionic acids the alkoxyl radical is replaced, the corresponding amides being formed. Thus, Klimenko [1] prepared α,α-dichloropropionamide by treating ethyl α,α-dichloropropionate with dilute ammonia at room temperature. Otto [3] prepared β,β-dichloropropionamide thru the reaction of concentrated aqueous ammonia with ethyl β,β-dichloropropionate in the cold.

Up to now, however, α,β-dichloropropionamide has not been described in the literature. As we showed earlier [4], when methyl α,β-dichloropropionate reacts with ammonia at room temperature or lower (down to -25°), chlorine is split off with separation of ammonium chloride, and, instead of the expected α,β-dichloropropionamide, a polymer of low molecular weight $(C_3H_5O_2N)_n$, is formed as final product.

Synthesis of α,β-Dichloropropionamide

A 20.0 g quantity of α,β-dichloropropionitrile [5], 50 g of 85% sulfuric acid, and 0.1 g of hydroquinone were stirred in a 100-ml, round-bottom flask for 24 hours at 18°, 24 hours at 40°, and 2 hours at 60°. The ice-cooled reaction mixture was neutralized with concentrated sodium carbonate solution, the sodium sulfate filtered out, and the aqueous solution extracted with ether. The ether was removed in vacuo, and α,β-dichloropropionamide was isolated in theoretical yield in the form of white crystals with m.p. 103° (from benzene).

Solubility of α,β-Dichloropropionamide at 20°

Solvent	Quantity of α,β-dichloropropionamide (in g) soluble in 100 g of solvent
Acetone	114.5
Methanol	89.2
Dioxane	76.2
Ethanol	31.1
Ether	19.3
Water	4.35
Chloroform	4.00
Benzene	1.98
Petroleum ether (b.p. 68°)	0.59
Hexane	0.44

At room temperature α,β-dichloropropionamide is very soluble in water, methanol, ethanol, ether, and dioxane and less soluble in benzene and hexane. Data on the solubility of α,β-dichloropropionamide are given in the table. Solutions of α,β-dichloropropionamide, falling on the skin, produce burns and blisters [6].

SUMMARY

A method of synthesizing α,β-dichloropropionamide and the properties of the latter are described.

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SOME REACTIONS OF CARBON SUBOXIDE

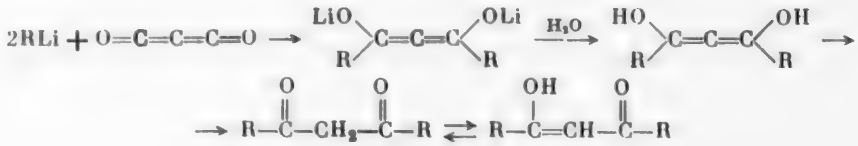
III. ORGANOLITHIUM SYNTHESIS OF SYMMETRICAL β-DIKETONES USING CARBON SUBOXIDE

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As was described in previous work [1], the use of carbon suboxide in organomagnesium synthesis leads to the formation of symmetrical β-diketones in a series of cases. The present investigation showed that organolithium synthesis may be used successfully for a similar purpose.

In all probability an organometallic compound adds to carbon suboxide at a carbonyl group and not at an ethylene link, since the density of the electron cloud at the oxygen atom is undoubtedly higher. The proposed reaction scheme is as follows:



EXPERIMENTAL

For the reactions we used ether solutions of carbon suboxide prepared by Staudinger's method [2]. The organolithium compounds required were prepared in metallation of alkyl halides in an atmosphere of nitrogen freed from impurities [3].

Preparation of Diacetylmethane. To a freshly prepared ether solution of 1.9 g of methyllithium was added 400 ml of an ether solution of carbon suboxide (2.80 g of C_3O_2). A light yellow precipitate formed rapidly and when it had settled, it was collected and treated with dilute sulfuric acid to weakly acid reaction to Congo Red. The liquid mixture was extracted three times with ether. After removal of the ether from the combined ether extracts, a fraction (1.9 g) with b.p. 133-135° (according to literature data diacetylmethane had b.p. 135-136° [4]), $n^{20}D$ 1.4538, and d_4^{20} 0.9696 was collected. A qualitative reaction for an enol grouping with ferric chloride was positive. Reaction of semicarbazide and the diacetylmethane yielded the amide of 3,5-dimethylpyrazole-1-carboxylic acid with m.p. 111-112°, which corresponds to literature data [4]. The yield of diacetylmethane calculated on the carbon suboxide was 47%.

Dipropionylmethane was obtained analogously to the previous compound. 1.9 g of ethyllithium and an ether solution of 1.4 g of carbon suboxide were used for the reaction. We collected a fraction with b.p. 74-75° (25 mm). According to literature data dipropionylmethane has b.p. 80° (30 mm) [5], $n^{20}D$ 1.4054 d_4^{20} 0.9442. A reaction for an enol grouping was positive. The amide of 3,5-diethylpyrazole-1-carboxylic acid had m.p. 134-135°, which corresponds to literature data. The yield of dipropionylmethane calculated on carbon suboxide was 60.4%.

Divalerylmethane was obtained by the action of an ether solution of 1.4 g of carbon suboixde on an ether solution of 2.9 g of butyllithium. We synthesized 2.2 g of divalerylmethane with b.p. 110-113° (20 mm), $n^{20}D$ 1.4564, d_4^{20} 0.9258. A reaction for an enol grouping was positive. The amide of 3,5-dibutylpyrazole-1-carboxylic acid had m.p. 166-168°. Our data agreed with that in the literature [6]. The yield of divalerylmethane calculated on carbon suboxide was 67%.

Dibenzoylmethane was obtained by the action of an ether solution of 3.2 g of phenyllithium on 200 ml of an ether solution of 1.45 g of carbon suboxide. Acid hydrolysis of the intermediate lithium compound, extraction with ether and removal of the latter yielded a crystalline product with m.p. 76-78°, which corresponds to literature data for dibenzoylmethane [7]. The reaction for an enol grouping was positive. We prepared the amide of 3,5-diphenylpyrazole-1-carboxylic acid with m.p. 202-203°, which does not disagree with literature data [4]. The yield of dibenzoylmethane was 2.9 g, which represents 60% calculated on the carbon suboxide.

Di(phenylaceto)methane was obtained from ether solutions of 5.0 g of benzyllithium and 1.6 g of carbon suboxide. We obtained 1.2 g of product with m.p. 52-53° (from ethanol) [1]. A reaction for an enol group was positive. With semicarbazide, di(phenylaceto)methane gave a substance with m.p. 177-180°, which in all probability was the amide of 3,5-dibenzylpyrazole-1-carboxylic acid.

Found %: N 14.27. M 307.6. $C_{18}H_{17}ON_2$. Calculated %: N 14.50. M 302.

The yield of di(phenylaceto)methane calculated on carbon suboxide was about 20%.

SUMMARY

1. It was shown that as a result of the interaction of carbon suboxide with organolithium compounds in the cold in diethyl ether, symmetrical aliphatic and aromatic β-diketones were formed.

2. The organolithium synthesis of symmetrical β-diketones led to somewhat higher yields than organomagnesium synthesis.

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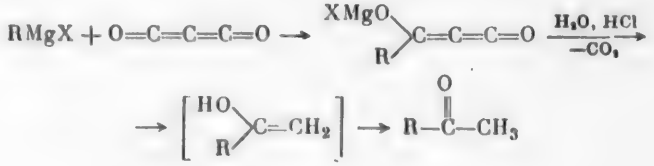
SOME REACTIONS OF CARBON SUBOXIDE

IV. INTERACTION OF CARBOCYCLYLMAGNESIUM HALIDES WITH CARBON SUBOXIDE

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In accordance with previous investigations [1, 2] it might have been expected that the reaction between carbocyclylmagnesium halides and carbon suboxide would have led to the formation of symmetrical β-diketones. However, the reactions of cyclopentylmagnesium and cyclohexylmagnesium bromides and of methylmagnesium and bornylmagnesium chlorides with carbon suboxide gave methyl ketones as the final products. The reactions apparently proceeded according to the following scheme:



EXPERIMENTAL

Ether solutions of carbon suboxide were obtained by Staudinger's method [3]. Cyclopentylmagnesium and cyclohexylmagnesium bromides [4] and methylmagnesium and bornylmagnesium chlorides [5] were also obtained by known methods.

Methyl Cyclopentyl Ketone. To an ether solution of cyclopentylmagnesium bromide, obtained from 3.7 g of cyclopentyl bromide, was added an ether solution of 0.5 g of carbon suboixde. When it had stood for a time, the reaction mixture was boiled gently on a water bath for 1 hour. The intermediate magnesium compound was then decomposed with 10% hydrochloric acid. The ether layer was separated and the aqueous one extracted three times with ether. The combined ether extracts were dried with baked sodium sulfate, the ether removed and the residue vacuum distilled. We obtained a fraction with b.p. 64-66° (10 mm), which corresponds to literature data for methyl cyclopentyl ketone [6], d_4^{20} 0.9161 and $n^{20}D$ 1.4452. The yield was 0.63 g (68%).

Found %: C 75.51; H 10.62. M 107.2. $C_7H_{12}O$. Calculated %: C 75.0; H 10.8. M 110.1.

Semicarbazone: m.p. 145-146° (from methanol).

Methyl Cyclohexyl Ketone. To an ether solution of cyclohexylmagnesium bromide, prepared from 3.4 g of cyclohexylmagnesium bromide, was added an ether solution of 0.5 g of carbon suboxide. Processing of the reaction mixture and isolation of the ketone were as in the previous case. We isolated a fraction with b.p. 64-65° (9 mm), which corresponds to literature data for methyl cyclohexyl ketone [7], d_4^{20} 0.8910, and $n^{20}D$ 1.4571. The yield was 0.6 g.

Found %: C 77.01; H 12.64. M 127.1. $C_8H_{14}O$. Calculated %: C 76.33; H 12.67. M 126.2.

Semicarbazone: m.p. 175-177° (from methanol).

Methyl menthyl ketone was obtained analogously to the previous ketone from 11.2 g of menthyl chloride and 0.5 g of carbon suboxide.

M.p. 147-148° (19 mm), d_4^{20} 0.9381, $n^{20}D$ 1.4900, MR_D 54.31; calc. 54.52.

Found %: C 78.82; H 12.30. M 183.19. $C_{12}H_{22}O$. Calculated %: C 79.07; H 12.10. M 182.4.

In accordance with the course of the synthesis and the data presented it can be assumed that we synthesized methyl methyl ketone. The yield was 3.2 g (61%).

Semicarbazone: m.p. 202-203° (from methanol).

Methyl bornyl ketone was obtained from 4.0 g of bornyl chloride and 0.5 g of carbon suboxide similarly to the previous compound.

B.p. 150-152° (20 mm), d_4^{20} 0.9470, $n^{20}D$ 1.4503, MR_D 56.12; calc. 56.64.

Found %: C 79.30; H 11.31. M 180.9. $C_{12}H_{19}O$. Calculated %: C 79.95; H 11.72. M 180.4.

In accordance with the course of the synthesis and the data presented it can be assumed that we synthesized methyl bornyl ketone. The yield of methyl bornyl ketone was 0.76 g (58%).

Semicarbazone: m.p. 195-196°.

Methyl menthyl ketone and methyl bornyl ketone are not described in the literature.

SUMMARY

The reaction between carbocyclylmagnesium halides (cyclohexylmagnesium and cyclopentylmagnesium bromides and methylmagnesium and bornylmagnesium chlorides) and carbon suboixde proceeded in a ratio of one molecule to one molecule and led to the formation of the corresponding methyl ketones.

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CONDENSATION OF ALDEHYDES AND KETONES

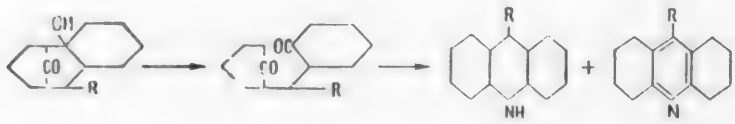
V. SYNTHESIS OF 9-PHENYLPERHYDROACRIDINE BY THE ACTION OF FORMAMIDE ON PHENYLTRICYCLOHEXANOLONE

M. N. Tilichenko and V. G. Kharchenko

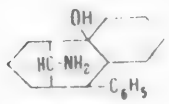
Saratov State University

In a recent communication from one of us and Vysotskii [1] a description was given of the action of formamide on tricyclohexanolone (I), which is the simplest representative of a new group of carbonyl-bridged ketols synthesized in our laboratory by diketone condensation of cyclohexanone with aldehydes [2-4].

When heated with formamide, ketol (I) first isomerized into 1,5-diketone (III) and the latter then reacted with formamide to give perhydro-(V) and sym-octahydro-(VII) acridines [1].



Phenyltricyclohexanolone (2-phenyl-3,4-tetramethylenebicyclo-[3,3,1]-nonanon-9-ol-4), which was readily obtained by condensation of cyclohexanone with benzaldehyde [3] and also with monobenzalcyclohexanone [3], obeyed the same rules when heated with formamide: instead of the normal possible hydroxyamine (VIII), it gave an almost quantitative yield of 9-phenylperhydroacridine (VI). It is curious that here we did not observe the formation of the corresponding octahydroacridine, as was the case with ketol (I). Whether it was caused by the effect of the C_6H_5 group or some difference in the reaction conditions has not been determined as yet.



(VIII)

The structure of 9-phenylperhydroacridine was confirmed by its catalytic dehydrogenation to 9-phenylacridine by Pd/C. Although it required a comparatively high temperature (~320°), the reaction proceeded quite smoothly and was sufficiently quantitative to serve as an identification of this hydroacridine by the volume of hydrogen liberated (6.6 moles was collected as compared with the theoretical amount of 7 moles).

EXPERIMENTAL*

Interaction of Phenyltricyclohexanone (II) with Formamide. We present a description of a typical experiment: 20 g of phenyl ketol with m.p. 207.5-208.5° and 25 ml of formamide** were heated in a round-bottomed flask with a reflux condenser and a thermometer reaching almost to the bottom of the flask. As the mixture was heated, there was a voluminous evolution of gas bubbles and gradual solution of the ketol; it had dissolved com-

*With the participation of student A. N. Karmashova.

**See [5] for preparation method.

pletely at 160°. The mixture was heated at 160-170° for 2 hours. On cooling the reaction mixture set to a slightly greyish, solid, crystalline paste. Under the microscope the crystals appeared as colorless, right cubes. The crystalline product was sucked off on a glass filter, washed several times with water and dried on a porous plate. The weight of the air-dried crystals, which corresponded to N-formyl-9-phenylperhydroacridine ($C_{19}H_{26}N \cdot HCO$), was 18.5 g and they had m.p. 194-195° (from dioxane). The crystals dissolved in alcohol, benzene and dioxane and were insoluble in water.

Found %: N 4.92, 4.85; HCO 9.61. $C_{20}H_{27}ON$. Calculated %: N 4.71; HCO 9.76.

The filtrate was combined with the wash waters and made alkaline with a 50% aqueous solution of NaOH to liberate 2 g of a white precipitate corresponding to 9-phenylperhydroacridine.

9-Phenylperhydroacridine (VI). N-Formyl-9-phenylperhydroacridine was readily hydrolyzed by heating on a water bath with 0.3 N NaOH in alcohol; dilution with water precipitated long, colorless platelets of the free base. The m.p. was 145-146° (from acetone). The 2 g of 9-phenylperhydroacridine liberated from the filtrate and wash waters also crystallized from acetone in the form of long platelets with m.p. 145-146°.

Found %: C 85.41, 85.46; H 10.48, 10.47; N 5.51, 5.35. M 287, 282. $C_{19}H_{27}N$. Calculated %: C 84.75; H 10.07; N 5.20. M 269.

The picrate was readily formed by mixing hot alcohol solutions of the base and picric acid. The yellow crystalline powder had m.p. 214-215° (from methanol).

Found %: N 11.30, 10.92. $C_{25}H_{30}O_7N_4$. Calculated %: N 11.05.

Phthalylation. 0.35 g of base in 2 ml of dioxane was mixed with 0.3 g of phthalic anhydride in 5 ml of dioxane. The slightly turbid mixture was heated on a water bath until it cleared. On cooling, the solution deposited a voluminous crystalline precipitate, which was collected, washed with dioxane and dried on an earthenware plate. The yield was 0.4 g and the m.p. 245-246° (from dioxane).

Found %: C 77.66, 77.85; H 7.77, 7.83. $C_{27}H_{31}O_3N$. Calculated %: C 77.70; H 7.43.

Dehydrogenation of 9-Phenylperhydroacridine to 9-Phenylacridine. 3.35 g of base and 1 g of Pd/C* was heated in a round-bottomed flask with a long neck attached to a gasometer. Hydrogen evolution began at 266° and was complete at 320°. 1.85 liter of hydrogen (0°, 760 mm) was liberated and this corresponds to 0.083 mole of H_2 as compared with the theoretical amount of 0.087 mole. The partly sublimed 9-phenylacridine deposited on the walls of the flask as large, green prisms, which were extracted mechanically. The caked mass remaining on the bottom of the flask was extracted with ether. The extract was filtered free from catalyst. Evaporation of the ether left a soft, clear, green mass containing needlelike crystals. When stirred with cold alcohol, the mass became a granular solid. Recrystallization from alcohol yielded yellow, needlelike crystals. The m.p. was 179.5-180.5°. A mixture with authentic 9-phenylacridine, synthesized from diphenylamine and benzoic acid [7] melted without depression. The total yield of 9-phenylacridine obtained was 3 g (95.2%).

Found %: C 89.39, 89.44; H 5.10, 5.23; N 5.41, 5.62. $C_{19}H_{13}N$. Calculated %: C 89.41; H 5.09; N 5.49.

SUMMARY

1. It was shown that the action of formamide on phenyltricyclohexanolone converted the latter almost quantitatively into 9-phenylperhydroacridine, which has not been described in the literature previously.

2. It was shown that 9-phenylperhydroacridine was almost quantitatively dehydrogenated to 9-phenylacridine in the presence of Pd/C.

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ULTRAVIOLET-ABSORPTION SPECTRA OF 3-HYDROXY-γ-PYRONE DERIVATIVES

G. A. Tolstikov

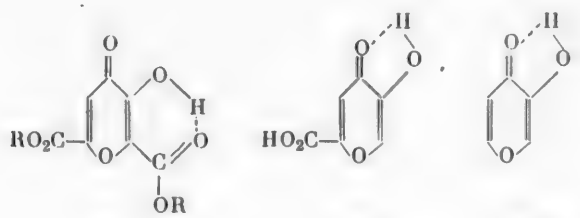
Institute of Chemical Sciences Academy of Sciences Kazakh SSR

There is little information in the literature on the spectroscopy of γ-pyrones [1-3]. Oxonium compounds of γ-pyrones have been studied more in this respect [4-6]. The absorption spectra of γ-pyrones should consist of high-intensity bands characterizing electron transitions in a conjugated system of π-bonds ($\pi\pi^{\#}$ transitions) and low-intensity bands caused by a p-$\pi^{\#}$ transition in the carbonyl group.

We investigated the absorption spectra of 3-hydroxy-γ-pyrone, comenic acid, ethyl comenate, ethyl methoxycomenate, meconic acid and its diethyl ester and diethyl ethoxymeconate. The substances were purified by repeated recrystallizations from suitable solvents to constant melting points. The absorption spectra were measured on an SF-4 spectrophotometer for water, ether and n-heptane solutions. The concentrations of the heptane solutions were 10^{-3} M and of the water and ether ones, 10^{-2} M. We paid most attention to establishing the character of the intramolecular hydrogen bonds in various hydroxypyrone derivatives and also to elucidating the effect of solvents on their absorption spectra, which has not been examined at all in previously published work.

To eliminate the effect of hydroxyls of the carboxyl groups, the acids were esterified. The results of the measurements are presented in the table and in Figs. 1-4.

On the basis of a comparative study of the reactivity of the hydroxyl and carboxyl groups in meconic (I) and comenic (II) acids and hydroxypyrone (III), it was previously shown that the following intramolecular hydrogen bonds existed [7]:



(I) (II) (III)

Spectral data made it possible to study this problem in more detail.

As is known the formation of a hydrogen bond is accompanied by a change in the absorption spectrum: the π-$\pi^{\#}$ bands of electron transitions undergo a bathochromic shift, while p-$\pi^{\#}$ bands are shifted in the opposite directions [8-10].

In most cases we studied the shifts of π-$\pi^{\#}$ bands,* since determining the position of the absorption maxima of p-$\pi^{\#}$ bands involved difficulties due to the masking effect of the high-intensity π-$\pi^{\#}$ bands. The presence of an intramolecular hydrogen bond in the hydroxypyrone molecule forming a five-membered ring produced a shift in the π-$\pi^{\#}$ band in the spectrum in heptane solution by 100 A° in comparison with methoxypyrone. The shift in

*Later on we will consider shifts in bands in the region of 200-300 mμ for comenic and meconic acid derivatives.

Expt. No.	Substance examined	Melting point	λ_{max}, in mμ								
			heptane			water			ether		
			λ^1 *	λ^2	λ^3	λ^1	λ^2	λ^3	λ^1	λ^2	λ^3
1	3-Hydroxy-γ-pyrone	117°	268 **, 3.95	—	—	270, 3.92	—	—	268, 3.95	—	—
2	3-Methoxy-γ-pyrone	85	258, 3.96	—	310—350, 1.60	270, 3.98	—	—	—	—	—
3	Comenic acid	275	—	—	—	224 ***, 4.32	290, 3.76	—	—	—	—
4	Ethyl comenate	127	240, 3.85	298, 3.60	—	246, 3.85	300, 3.63	370, 1.50	240, 3.85	302, 3.62	—
5	Ethyl methoxycomenate	156	—	—	—	226, 4.36	296, 3.66	—	242, 3.82	287, 3.63	360
6	Meconic acid	255	—	—	—	236, 4.13	306 ****, 3.91	—	—	—	—
7	Diethyl meconate	111	236, 4.03	302, 3.90	370	238, 4.10	307, 3.90	—	—	—	—
8	Diethyl ethoxymeconate	61	282, 3.80	—	—	288, 3.88	—	—	—	—	—

* λ^1_{max} and λ^2_{max} denote the positions of the maxima of π-π# bands and λ^3_{max}, those of p-π# bands.

** The second number in the column corresponds to lg k.

*** The increase in the number of π-π# bands in comparison with hydroxypyrone may be explained by the lengthening of the conjugation chain of π-bonds with the introduction of a carboxyl group.

**** The clearer appearance of the short-wave band in comparison with comenic acid is due to the introduction of yet another carboxyl group.



Fig. 1. 1) Methoxypyrone in heptane, 2) the same in water, 3) hydroxypyrone in heptane, 4) the same in water.

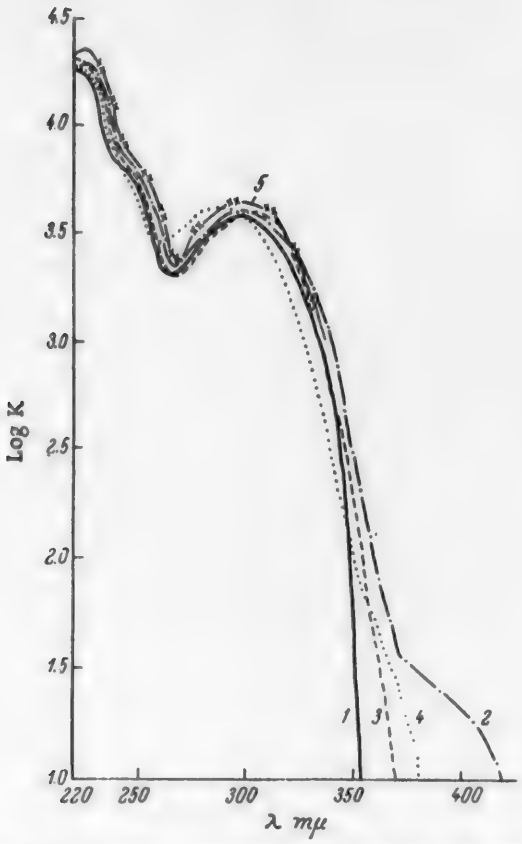


Fig. 2. 1) Comenic ester in heptane, 2) the same in water, 3) the same in diethyl ester, 4) methoxycomenic ester in diethyl ether, 5) the same in water.

the band of the $\pi-\pi^{\#}$ transition toward longer wavelengths and in the band of the $p-\pi^{\#}$ transition in the opposite direction led to the latter being masked by the strong $\pi-\pi^{\#}$ band and it did not appear in the spectrum.

Alkylation of the hydroxyl group excluded participation of the carbonyl in the hydrogen bond and due to this the band of the $p-\pi^{\#}$ transition was expressed so clearly in the spectrum of a heptane solution that a vibration structure appeared.*

In the case of comenic ester and its methoxy derivative, the shift in the maximum of the $\pi-\pi^{\#}$ band was 110 A°. As in the case of hydroxypyrone, this shift was caused by the existence of an intramolecular hydrogen bond in the comenic acid molecule, joined to the carbonyl of the nucleus. The slightly greater value of the shift in comparison with that for hydroxypyrone, however, did not mean that the hydrogen bond was stronger in comenic acid. This problem will be discussed below. The band of the $p-\pi^{\#}$ transition in the spectrum of a heptane solution of comenic ester was not expressed for the same reason as in the case of hydroxypyrone.

The greatest shift in a $\pi-\pi^{\#}$ band of 200 A° was observed with the diethyl esters of meconic and ethoxymeconic acids, i.e.,the strength of the hydrogen bond in meconic acid was greater than in the case of hydroxypyrone and comenic acid.

The shift in the absorption band on going from heptane to water was 50 A° for ethyl meconate, i.e. greater than the analogous shifts for hydroxypyrone and comenic ester. This is only possible when the carbonyl is free from intramolecular interaction and forms a hydrogen bond with water.

* The average difference between "peaks" was 1225 cm^{-1}.

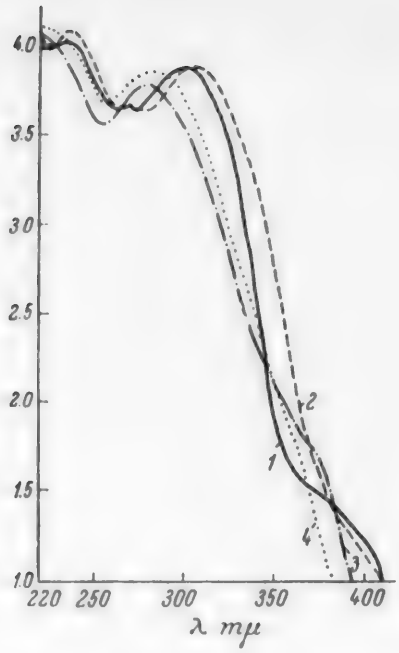


Fig. 3. 1) Meconic ester in heptane, 2) the same in water, 3) ethoxymeconic ester in heptane, 4) the same in water.

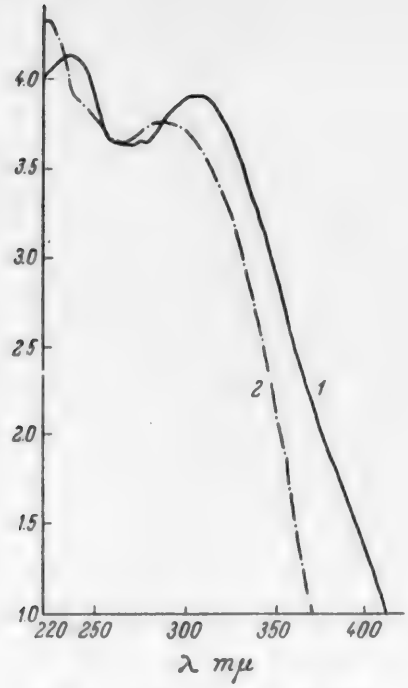


Fig. 4. 1) Meconic acid in 96% C_2H_5OH, 2) comenic acid in water.

The band of the p-$\pi^{\#}$ transition was clearly expressed in the spectrum of a heptane solution of meconic ester, indicating, on the one hand, the nonparticipation of the carbonyl in the intramolecular hydrogen bond and, on the other hand, the strong acceptor action of the carbethoxy groups facilitating the transfer of the unshared electrons of the carbonyl oxygen to the π^{*}-orbit. The diffuseness of the bands of the p-$\pi^{\#}$ transition in the spectrum of an aqueous solution was caused by interaction of water with the carbonyl.

The presence of bathochromic shifts in the π-$\pi^{\#}$ bands on going from heptane to aqueous solutions indicates partial rupture of the intramolecular bonds by water. The spectrum of an aqueous solution of comenic ester showed a p-$\pi^{\#}$ band, which was absent from the spectrum of a heptane solution. Apparently, due to its unshared pair, water reacts with the hydroxyl of comenic ester. The carbonyl, whose negativity is strongly reduced, is largely free from interaction.

It should be pointed out that the negativity of the carbonyl falls strongly in the series hydroxypyrone – comenic acid – meconic acid. This is confirmed by the values of the shifts in the π-$\pi^{\#}$ bands in going from heptane to aqueous solutions of alkoxy derivatives. These shifts respectively equalled: methoxypyrone 120 A°, methoxycomenic ester 90 A° and ethoxymeconic ester 60 A°.

For a conclusive demonstration of the difference in the affinities of the hydroxyls of hydroxypyrone and comenic ester for carbonyl, we measured the absorption spectra of their solutions in diethyl ether. The spectrum of an ether solution of hydroxypyrone almost completely coincided with the spectrum of its heptane solution.

In the case of comenic ester, there was a bathochromic shift of 40 A° in going from heptane to ether solution. This was apparently the result of interaction of the diethyl ether oxygen with the hydroxyl of comenic ester.

The author is very grateful to Yu. A. Kushnikov for valuable advice.

SUMMARY

1. The ultraviolet spectra of hydroxypyrone, methoxypyrone, comenic acid, the ethyl esters of comenic and methoxycomenic acids, meconic acid and its diethyl ester and diethyl ethoxymeconate in neutral and polar solvents were measured.

2. It was established that it was possible to write the following series according to the fall in the strength of the intramolecular hydrogen bond: meconic acid > hydroxypyrone > comenic acid.

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OXIDATION – REDUCTION SYSTEMS FOR INITIATION OF RADICAL PROCESSES

X. THE MECHANISM OF ACTION OF OXIDATION – REDUCTION SYSTEMS INVOLVING SO_2

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The dual nature of SO_2 makes it possible to use this substance in oxidation – reduction systems in conjunction with both oxidants (peroxides and hydroperoxides) and with reductants (mercaptans, hydrogen sulfide and dienoles). As we showed, these systems may be used for the initiation of radical processes in hydrocarbon media [1,2]. In the present communication we present experimental data making it possible to consider the mechanism of action of this type of system.

a) System Containing Isopropylbenzene Hydroperoxide and SO_2. The reaction between isopropylbenzene hydroperoxide and SO_2 in hydrocarbon solutions proceeds at a very great rate and produces rapid gel formation in rubber solutions [1]. On studying this reaction, the hypothesis was put forward that structuralization was caused by the formation of free radicals in an intermediate stage in the reaction:

$$1.\ ROOH + SO_2 \rightarrow RO\cdot + \cdot(SO_2H).$$

The character of the intermediate reaction products could be established by the use of acceptors capable of interacting with free radicals. The reaction of free aliphatic and some hetero radicals with α-olefins proceeds largely through addition at the double bond with the formation of the corresponding products [3, 4]. The $\cdot(SO_2H)$ radical may have a reactive center at the sulfur atom $\cdot S(=O)(OH)=O$ or at an oxygen atom $HO-S(=O)=O\cdot$. In the first case its addition to an olefin leads to the formation of a sulfonic acid [equation (2)] and in the second, to the formation of sulfo esters [equation (3)].

$$2.\ CH_2=CHX + \cdot SO_3H \rightarrow HO_3SCH_2-\dot{C}HX,$$

$$3.\ CH_2=CHX + O=S(OH)(O\cdot) \rightarrow HO_2SOCH_2-\dot{C}HX.$$

These and other groups in the addition products are determined as sulfonic acids by titration with alkali.

We chose styrene as a free radical acceptor. The reaction was carried out at 0 and -17° with excess SO_2 (8-11 moles of SO_2 per mole of hydroperoxide). To avoid the formation of sulfuric acid (the final product of SO_2 oxidation), a solution of hydroperoxide in styrene was slowly added to a solution of SO_2 in styrene so that the process was carried out with a constant excess of SO_2.* The reaction was performed in a nitrogen atmosphere

*In our laboratory, T. N. Kuren'gina showed that when the reaction was carried out with excess hydroperoxide (gradual addition of SO_2 to a solution of isopropylbenzene hydroperoxide in cumene) a very small amount of H_2SO_4 and RSO_3H was formed and as is known, the latter produce catalytic decomposition of the hydroperoxide to phenol and acetone. Phenol, characterized as tribromophenol, was isolated in about 90% yield. The reaction was accompanied by complete consumption of the hydroperoxide; the bulk of the SO_2 was recovered unchanged.

TABLE 1

Interaction of Isopropylbenzene Hydroperoxide with SO_2 in Styrene Solution

Temperature	Content in starting mixture per 50 ml of styrene (mole)		Yield of polysulfone (in g)	S content of polysulfone (in %)	No. of moles of SO_2 reacted per mole of hydroperoxide	No. of moles of styrene per mole of SO_2 in polysulfone	SO_3H content of polysulfone (in % of theoretical*)
	SO_2	hydroperoxide					
0°	0.055	0.005	12.8	7.4	6.15	3.8	68
0	0.050	0.005	13.8	9.0	7.8	2.8	99
-17	0.072	0.009	18.8	10.1	6.7	2.4	90

*The amount of SO_3H formed according to reactions (1) and (2) was taken as the theoretical value.

TABLE 2

Interaction of Isopropylbenzene Hydroperoxide with SO_2 in Styrene Solution in the Presence of Nitric Oxide (-17°)

Expt. No.	Content in starting mixture per 100 ml of styrene (mole)		Yield of polysulfone (in g)	SO_2 found (in % of theoretical**) in the form of	
	SO_2	hydroperoxide		H_2SO_4	RSO_3H
1	0.144	0.015	0	0	15.9
2	0.236	0.113	0	4.1	37.2
3	0.30	0.100	0	10.9	37.1

**As the theoretical values we took the amount of RSO_3H formed according to equations (1) and (2) and the amount of H_2SO_4 formed according to the equation $RO\cdot + \cdot SO_3H \rightarrow ROH + SO_3$.

with the reaction mixture stirred continuously. The interaction of hydroperoxide with SO_2 proceeded at a great rate and was accompanied by a rise in temperature. Even after the addition of the first drops of hydroperoxide solution, the formation of a white precipitate of polysulfone began. At the end of the process the reaction mixture was a solid mass of polysulfone, swollen with styrene monomer. Analysis showed complete consumption of the hydroperoxide and the absence of H_2SO_4 and soluble sulfonic acids. The SO_2 did not react completely.

The polysulfone obtained, freed from unpolymerized styrene and SO_2, appeared as a white powder, which was soluble in pyridine and a mixture of pyridine and acetone, but insoluble in aliphatic and aromatic solvents. The product was analyzed for sulfur and SO_3H group content. The experimental data presented in Table 1 show that there were 2.5-3.5 moles of styrene in the polysulfone per mole of SO_2, i.e., the polysulfone obtained was a copolymer of styrene and SO_2 similar to the copolymers formed by the interaction of SO_2 with olefins in the presence of radical polymerization initiators [5, 6].

From the data on the sulfur content and the weight of the polysulfone we calculated the amount of SO_2 which reacted. In most experiments 6-8 moles of SO_2 reacted for each mole of hydroperoxide introduced. Consequently only about 15% of the SO_2 which reacted was consumed in initiation under the chosen conditions; the rest of it was involved in the process due to the chain polymerization reaction. In addition to SO_2, SO_3H groups were shown to be present in the polysulfone and their content was 70-100% of theoretical. The presence of SO_3H groups in the polysulfone is a direct indication that the reaction between the components of the system proceeded with the formation of $\cdot(SO_3H)$ free radicals. The radical chain character of polysulfone formation was demonstrated by the inhibiting action of nitric oxide on this process. When the reaction was carried out under the same

TABLE 3

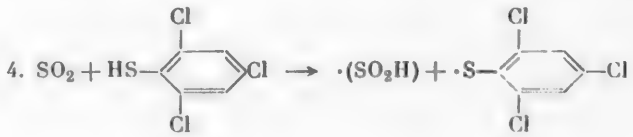
Content of Trichlorothiophenol and SO_2 Fragments in Polymer in Relation to the Composition of the Starting Mixture

Experimental conditions	RSH : SO_2 in starting mixture (in moles)	Content in polymer (in moles)		Remarks
		RSH	SO_2	
In a nitrogen medium	1 : 33	0.055	0.02	Gel
The same	1 : 104	0.035	0.105	The same
In the presence of nitric oxide	1 : 35	0.0117	0.0008	No gel. The polymer contained 0.64% nitrogen

conditions with nitric oxide passed through the solution continuously, the hydroperoxide was consumed completely but no polysulfone was formed. The reaction product was a mixture of sulfonic acids and sulfuric acid (see Table 2).

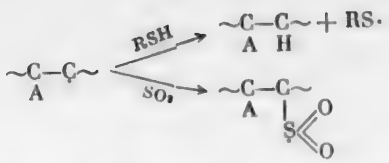
Nitric oxide reacted quantitatively with free radicals with a reaction center at a carbon atom, which led to complete suppression of the chain process of polysulfone formation. In the case of radicals of the type RO· or ·(SO_2H), formed by reaction of hydroperoxide with SO_2, the reaction with NO is less probable due to the low energy of the O-N and S-N bonds. This apparently explains the fact that ·(SO_2H) radicals were not quantitatively trapped and due to this considerable amounts of sulfonic acids (products of the addition of SO_2H to styrene) were found in the reaction products.

b) System Containing SO_2 and Trichlorothiophenol. It was shown previously that the reaction between trichlorothiophenol and SO_2 produces the vulcanization of rubbers at low temperatures [2]. The structuralization of rubbers was accompanied by the addition of trichlorothiophenol and SO_2 fragments to the unsaturated polymer chain. It was proposed that the initiation of polymer structuralization was connected with the formation of free radicals [2].



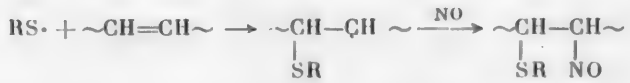
4. $SO_2 + HS-C_6H_3Cl_2 \rightarrow \cdot(SO_2H) + \cdot S-C_6H_3Cl_2$

In the present work we studied the structuralizing action of this system on solutions of the butadiene rubber SKB at room temperature with various ratios of SO_2 and trichlorothiophenol and the effect of nitric oxide on this process. The process was characterized by the effect of gel formation and the content of trichlorothiophenol and SO_2 fragments in the polymer at the end of the reaction. Data presented in Table 3 show that trichlorothiophenol was involved in the process much more than corresponded to its molar content in the starting mixture with SO_2. Even with a considerable excess of SO_2 in the mixture (33 moles per mole of thiophenol), the gel contained more trichlorothiophenol than SO_2 and the amount of SO_2 added exceeded the amount of trichlorothiophenol added only at a very large excess of SO_2 (104 moles per mole of trichlorothiophenol). Primary radicals A·, formed by interaction of trichlorothiophenol (RSH) with SO_2 (according to equation 4), added to the C=C bond and then a chain process began which was characterized by two competing reactions



The first reaction led to the addition of the mercaptan to the chain and the seond one, to the formation of sulfones. The results obtained indicate that the reaction proceeded mainly in the first direction, which agrees with the particular tendency of mercaptans (especially thiophenols) toward chain transfer acts.

No gel was formed when the reaction was carried out under the same conditions in the presence of nitric oxide. The polymer isolated contained considerably less mercaptan and hardly any SO_2. The chain stage of trichlorophenol and SO_2 addition was apparently suppressed completely.



After the reaction, the polymer was found to contain 1.28% of bound nitric oxide (on nitrogen). The experimental data obtained show that the reaction between SO_2 and trichlorothiophenol, leading to structuralization of the unsaturated polymers, is accompanied by addition of trichlorothiophenol and SO_2 to the polymer chain with a large number of trichlorothiophenol molecules added for each molecule of SO_2 reacting. The radical chain character of the reaction is also confirmed by the inhibiting action of nitric oxide on this process and its addition to the polymer chain.

EXPERIMENTAL

The styrene was freed from stabilizer (hydroquinone) by washing with 5% NaOH solution and water and vacuum distillation after drying over calcium chloride. The isopropylbenzene hydroperoxide was purified through the sodium salt. The product isolated contained 99.0% of hydroperoxide.

Analysis Procedures. The isopropylbenzene hydroperoxide was determined iodometrically after removal of the SO_2 from the system.

The soluble sulfonic acids and sulfuric acid were determined in the presence of each other by a procedure based on the different solubilities of the aniline salts of sulfuric acid and sulfonic acids [7].

The SO_3H group content of the polysulfone was determined by titrating a sample of polysulfone (about 1 g) dissolved in a mixture of pyridine and acetone with a 0.1 N alcohol solution of NaOH in the presence of phenolphthalein.

SUMMARY

1. It was shown that the reaction between isopropylbenzene hydroperoxide and SO_2 in styrene solution was accompanied by the formation of polysulfone. Nitric oxide completely inhibited this process. An examination of the products from the interaction of hydroperoxide with SO_2 in styrene in the presence of nitric oxide and without it showed that the reaction proceeded through the stage of $\cdot(SO_3H)$ radicals, which reacted with monomers to form sulfonic acids.

2. It was shown that the reaction between SO_2 and trichlorothiophenol, which led to structuralization of unsaturated polymers, proceeded by a chain mechanism and was accompanied by the addition of trichlorothiophenol and SO_2 to the unsaturated polymer chain. Nitric oxide inhibited this process.

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CONVERSIONS OF XYLENOLS ON AN ALUMINOSILICATE CATALYST

II. CONVERSION OF 1,2,4- and 1,3,4-XYLENOLS*

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When passed over an aluminosilicate catalyst, 1,2,4-, and 1,3,4-xylenols (like 1,3,5-xylenol) were partially converted into a mixture of cresols and phenol and partially into substances of a neutral character which began to boil at 113°. As in the case of 1,3,5-xylenol [1], toluene was not detected in the reaction products. In this case the neutral products consisted of xylene and trimethylbenzene isomers and neutral substances with b.p. above 185°. Carrying out the reaction in a stream of hydrogen chloride led to an increase in the amount of the phenol-cresol fraction and a decrease in the amount of neutral substances.

Conversion of a solution of 1,2,4- (or 1,3,4-) xylenol in benzene over an aluminosilicate catalyst at 350-450° yielded phenols and cresols and also neutral compounds with b.p. over 100°. It was established that the neutral products contained the same substances (toluene, o-, m- and p-xylenes, pseudocumene, mesitylene, durene and substances with b.p. over 200°) as in the case of 1,3,5-xylenol [1].

Comparison of the effects of contact temperature and time on the conversion of 1,3,5-xylenol and 1,2,4- and 1,3,4-xylenols in benzene solution showed that with an increase in contact temperature from 350 to 450° the amount of the phenol-cresol fraction decreased in all cases, while both the amount of neutral compounds with b.p. above 100° (including toluene) and the amount deposited on the catalyst increased. An increase in the contact time had an effect analagous to that of raising the temperature.

The results we obtained on the conversion of 1,3,5- 1,2,4- and 1,3,4-xylenols make it possible to consider their possible conversion routes over an aluminosilicate catalyst at 350-450°.

Evidently the main reactions were disproportionation and isomerizations (I), described by American investigators for cresols and xylenols over an aluminosilicate catalyst [2], and also the reduction of phenol and homologs (II).

$$2(CH_3)_2C_6H_3OH \rightleftarrows CH_3C_6H_4OH + (CH_3)_3C_6H_2OH,$$

$$(CH_3)_2C_6H_3OH \xrightarrow[-H_2O]{+2H} (CH_3)_2C_6H_4.$$

The addition of benzene led to a competing reaction, the transfer of a methyl group of a phenol homolog to a benzene molecule (III).

$$(CH_3)_2C_6H_3OH + C_6H_6 \longrightarrow CH_3C_6H_4OH + C_6H_5CH_3.$$

Evidently the dealkylation of phenol homologs occurred first and then their reduction. With an increase in the reaction temperature the rate of reduction of phenol homologs leading to the formation of benzene homologs increased much more rapidly than the rate of dealkylation of phenol homologs.

*The carbon atom bearing the hydroxyl group is given the number 1.

TABLE 1

Obtained (in % of original xylenol)	1,3,5-Xylenol			1,3,4-Xylenol			1,2,4-Xylenol		
	350°	400°	450°	350°	400°	450°	300°	400°	450°
Phenolic compounds	21.8	11.1	7.0	23.7	12.7	10.0	22.1	14.0	2.7
Including phenol-cresol fraction with b.p. 180-210°	8.1	9.1	5.4	16.2	11.8	8.0	10.0*	7.4	2.2
Neutral substances with b.p. above 100°	30.1	36.0	44.7	16.7	23.9	27.6	28.8	35.5	38.1
Including toluene	3.3	5.4	10.6	1.1	3.5	5.5	4.7	6.6	10.2
Deposited on catalyst	25.7	31.6	35.0	24.1	25.6	41.7	27.7	29.0	33.1
Xylenol converted**	86.3	98.0	98.4	92.5	99.1	98.0	87.9	93.4	99.5

*In the case of 1,2,4-xylenol a fraction with b.p. 180-203° was collected.

**In experiments with 1,3,5- and 1,2,4-xylenols the contact time was 85-95 sec. and in experiments with 1,3,4-xylenol, 110 sec.

TABLE 2

Obtained (in % of original xylenol)	1,3,5-Xylenol			1,3,4-Xylenol			1,2,4-Xylenol		
	22 sec	31-35 sec	87-95 sec	23-27 sec	36 sec	110 sec	22-24 sec	65 sec	85 sec
Phenolic compounds	33.6	20.2	7.0	44.7	16.9	10.0	41.1	29.1	2.7
Including phenol-cresol fraction with b.p. 180-210°	17.1	13.6	5.4	19.9	10.9	8.0	16.8*	11.5	2.2
Neutral substances with b.p. above 100°	43.0	49.5	44.7	28.6	36.4	27.6	34.5	35.1	38.1
Including toluene	3.1	7.7	10.6	4.0	2.7	5.5	2.1	2.6	10.2
Deposited on catalyst	11.2	20.1	35.0	11.9	19.7	41.7	9.4	19.6	33.1
Xylenol converted	83.5	93.4	98.4	75.2	94.0	98.0	75.7	82.4	99.5

* In the case of 1,2,4-xylenol a fraction with b.p. 180-203° was collected.

Thermodynamic calculations showed that analogous reactions occurred in the conversion of cresols under other conditions also (500-650° and a hydrogen pressure of 70 atm) [3].

Transfers of an alkyl group in benzene derivatives have been described in the literature. It has been reported that an isopropyl group is transferred from a diisopropylbenzene molecule to a benzene molecule under the action of activated clays [4]. Under the action of aluminosilicate at a temperature of not more than 450° an ethyl (isopropyl) group is transferred from a diethyl-(diisopropyl)-benzene molecule to a benzene molecule [5]. Smitt described the transfer of alkyl groups (tert -butyl and tert -amyl) from a p-alkylphenol molecule to a benzene molecule in the presence of aluminum chloride [6]. The transfer of a methyl group from a xylene molecule to a benzene molecule on aluminosilicate has been described by Hansford, Myers and Sachanen [7]. A series of investigations have recently been published by A. V. Topchiev, Yu. G. Mamedaliev and G. M. Mamedaliev et al. [8] on the dealkylation of xylenes and polymethylbenzenes and the conjugated alkylation of

benzene and toluene in the presence of a synthetic aluminosilicate catalyst. They showed that under the action of this catalyst a methyl group was transferred from a xylene (or polymethylbenzene) molecule to a benzene (toluene) molecule with the formation of toluene (or xylenes).

Our investigations on the interaction of xylenols with benzene on an aluminosilicate catalyst demonstrate the possibility of the transfer of a methyl group from the molecule of phenolic compounds also to a benzene molecule.

EXPERIMENTAL

Starting Materials. 1,2,4-Xylenol was obtained from 1,2,4-xylidine by the procedure described for the preparation of m-cresol from m-toluidine [9] and had b.p. 209.0-209.5° (747 mm) and m.p. 23.5°.

1,3,4-Xylenol was pure-grade (Kharkhov Chemical Reagent Factory) and had b.p. 225° (760 mm) and m.p. 59.5-60.3°.

Benzene and the aluminosilicate catalyst and also the experimental procedure treatment and identification of products were the same as in [1].

Conversion of 1,2,4-Xylenol over an Aluminosilicate Catalyst. During 3 cycles (3 hours each) 95.7 g of 1,2,4-xylenol was passed over the catalyst at 350°. The contact time was 73.8 sec. The increase in weight of the catalyst was 17.4 g (18.2%). Treatment of the catalyzate (70.2 g) yielded 26.4 g of phenols and 16.4 g of neutral substances. Distillation of the phenols yielded the fractions: 1st b.p. 180-198°, 6.8 g; 2nd b.p. 198-203°, 4.7 g; 3rd b.p. 203-211°, 4.0 g; 4th b.p. 211-217°, 5.3 g; residue 5.6 g.

The infrared-absorption spectra of the 1st and 2nd fractions were plotted and it was established that the 1st fraction contained o-cresol (absorption λ_{max} 13.37 μ); and a small amount of phenol (λ_{max} 9.29 μ); the 2nd fraction contained m-cresol (λ_{max} 12.96 μ) and p-cresol (λ_{max} 12.34 μ).

Distillation of the neutral substances yielded fractions: 1st b.p. 113-150°, 4.0 g; 2nd b.p. 150-185°, 3.1 g; residue 9.3 g.

Nitration of the 1st fraction [10] yielded light-yellow needles with m.p. 180-180.5°. A mixed melting point with 2,4,6-trinitro-m-xylene (m.p. 182°) was not depressed. Nitration of the 2nd fraction yielded a light-yellow substance with m.p. 169-171° which corresponded in composition to trinitrotrimethylbenzene (prisms of trinitropseudocumene and needles of trinitromesitylene were clearly visible under the microscope).

Found %: N 16.65, 16.78. $C_9H_9O_6N_3$. Calculated %: N 16.47.

Conversion of a Solution of 1,2,4-Xylenol in Benzene over an Aluminosilicate Catalyst. During 4 cycles (3 hours each) at 350° with a contact time of 64.1 sec, 62.0 g of 1,2,4-xylenol and 113.5 g of benzene were passed over the aluminosilicate catalyst. The increase in weight of the catalyst was 9.1 g (14.7%). Treatment of the catalyzate (158.5 g) yielded 23.2 g of phenols, 104.5 g of unchanged benzene and 14.7 g of neutral substances with b.p. above 100°.

Distillation of the phenols yielded the following fractions: 1st b.p. 183-203°, 9.2 g (14.9%); 2nd b.p. 203-211°, 8.9 g (14.3%); 3rd b.p. 211-217°, 2.3 g (3.8%); residue 2.8 g.

Plotting the infrared-absorption spectra of the 1st fraction showed the presence of o-, m- and p-cresols (absorption with λ_{max} 13.37, 12.98 and 12.34 μ, respectively) and a small amount of phenol (λ_{max} 9.29 μ). The m-cresol content of the 1st fraction was 20.7% (by Raschig's method).

Distillation of the neutral substances yielded fractions: 1st b.p. 100-113°, 1.6 g (2.5%); 2nd b.p. 113-147°, 2.0 g (3.3%); 3rd b.p. 147-185°, 0.6 g (1.1%); residue 10.5 g.

Nitration [10] of 0.2 g of the 1st fraction, which contained toluene, yielded 0.28 g of light-yellow needles with m.p. 70.0-70.5°. A mixed melting point with 2,4-dinitrotoluene was not depressed.

The 2nd fraction was oxidized with potassium permanganate by the procedure of Moldavskii et al. [11]. Phthalic anhydride with m.p. 130° (m.p. 131.6° in the literature) was isolated. The dimethyl esters of terephthalic and isophthalic acids (m.p. 136.5-138° and 55-56°, respectively) were obtained. Mixed melting points with authentic compounds were not depressed.

TABLE 3

Obtained (in % of original material)	1,2,4-Xylenol		1,3,5-Xylenol	
	without HCl	in an HCl atmosphere	without HCl	in an HCl atmosphere
	C.T.* 73.3 sec.	C.T. 67.8 sec.	C.T. 35.6 sec.	C.T. 40.7 sec.
Phenolic compounds	27.6	43.5	34.4	42.5
Including phenol-cresol fraction with b.p. 180-203°	10.1	16.4	3.4	4.2
Phenol-cresol fraction (in % of xylenol reacted)	12.5	22.5	4.4	6.1
Neutral compounds	17.1	15.3	40.0	27.4
Deposited on catalyst	18.2	13.8	13.1	15.6
Xylenol converted	82.5	72.9	77.1	69.2

*C.T. equals contact time.

Nitration of the 3rd fraction yielded a light-yellow substance with m.p. 166-168°, which corresponded to trinitrotrimethylbenzene in composition.

Found %: N 16.52, 16.33. $C_9H_9O_6N_3$. Calculated %: N 16.47.

Conversion of 1,3,4-Xylenol in Benzene Solution over an Aluminosilicate Catalyst. During 6 cycles (3 hours each) at 400° and with a contact time of 110 sec., 32.0 g of 1,2,4-xylenol dissolved in 112.6 g of benzene was passed over the aluminosilicate catalyst. The increase in weight of the catalyst was 8.2 g (25.6%). Treatment of the catalyzate (116.4 g) yielded 4.1 g of phenols, 93.0 g of unchanged benzene and 7.7 g of neutral substances with b.p. above 100°.

On distilling the phenols from a Favorskii flask, we collected fractions: 1st b.p. 183-203°, 2.0 g (6.3%); 2nd b.p. 203-210°, 1.8 g (5.5%); residue 0.3 g.

Distillation of the neutral substances yielded fractions: 1st b.p. 100-113°, 1.1 g (3.5%); 2nd b.p. 113-147°, 1.7 g (5.2%); 3rd b.p. 147-185°, 1.8 g (5.5%); residue 3.1 g.

The 1st fraction contained toluene and yielded 2,4-dinitrotoluene with m.p. 70.2-70.4° on nitration. Oxidation of the 2nd fraction with potassium permanganate yielded phthalic anhydride with m.p. 127.5-128.5° and also terephthalic and isophthalic acids, from which we obtained dimethyl esters with melting points 139-140° and 62-64°, respectively. Mixed melting points with authentic compounds were not depressed. Nitration of the 3rd fraction gave trinitromesitylene in the form of needles with m.p. 230-231° and trinitropseudocumene in the form of prisms with m.p. 181-182°. Mixed melting points with authentic trinitromesitylene (m.p. 232°) and trinitropseudocumene (m.p. 185°) were not depressed.

Effect of Temperature on Conversion of Xylenols. Experiments were carried out at 350, 400 and 450° in the presence of benzene. The results are presented in Table 1.

Effect of Volume Rate on Conversion of Xylenols. Experiments were carried out at 450° in the presence of benzene with contact times of from 22 to 110 sec. The results are given in Table 2.

Conversion of Xylenols in a Hydrogen Chloride Atmosphere. During 2 cycles (3 hours each) 30.8 g of 1,2,4-xylenol was passed over the catalyst at 350° with the simultaneous input of hydrogen chloride at a rate of 40 ml/min. Processing the catalyzate (28.4 g) yielded 13.4 g of phenols and 4.7 g of neutral substances.

Distillation of the phenols yielded the following fractions: 1st b.p. 183-203°, 5.0 g (16.4%); 2nd b.p. 203-211°, 2.7 g (8.8%); 3rd b.p. 211-217°, 2.5 g (7.9%); residue 3.2 g.

Distillation of the neutral substances yielded fractions: 1st b.p. 115-130°, 0.4 g (1.3%); 2nd b.p. 130-150°, 0.6 g (2.0%); 3rd b.p. 150-185°, 0.7 g (2.2%); residue 3.0 g.

An experiment on the conversion of 1,3,5-xylenol in the presence of benzene in an atmosphere of hydrogen chloride was carried out. The results are presented in Table 3.

SUMMARY

1. When passed over an aluminosilicate catalyst in the presence of benzene and in its absence, 1,2,4- and 1,3,4-xylenols underwent conversions analogous to 1,3,5-xylenol.

2. The effect of temperature, volume rate and the addition of hydrogen chloride on the conversion of xylenols was demonstrated.

3. Possible routes were put forward for the conversion of xylenols over an aluminosilicate catalyst at 350-450°.

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A CONTRIBUTION TO THE STUDY OF OXIDATIVE NITRATION OF AROMATIC COMPOUNDS

III. OXIDATIVE NITRATION OF ACETOXYMERCURI-p-XYLENE

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The conversion of aromatic compounds into nitrophenols under the action of a mixture of mercury nitrate and nitric acid of medium concentration proceeds through the formation of arylmercury nitrates and nitroso derivatives. According to Titov and Laptev, the latter are converted into nitrophenols through hypothetical p-hydroxyarylhydroxylamines and p-nitrosophenols and partially through aryldiazonium nitrates and phenols [1].

On treating p-xylene with 51% nitric acid in the presence of mercury nitrate at 28°, we did not find an appreciable amount of the expected nitrophenols [2]. Nitrophenols were not obtained either by the action of 58% nitric acid on acetoxymercuri-p-xylene at 20, 40 or 50°.

Subsequent investigations showed that temperature had a determining effect on the reaction. We were able to obtain dinitro-p-xylenol by oxidative nitration of acetoxymercuri-p-xylene and also p-xylene at low temperature only.

The action of 58% nitric acid containing oxides of nitrogen at 2-4° on acetoxymercuri-p-xylene, obtained by direct mercuration of p-xylene with mercuric acetate, gave a 23.8% yield of dinitro-p-xylenol, which was identical with the x,x-dinitro-2-hydroxy-p-xylene described in the literature [3].

When a reaction mixture obtained under analogous conditions was kept at 20-22° for 16 hours, the nitrophenols decomposed and dark colored, tarry products were formed. The latter apparently explains the absence of appreciable amounts of nitrophenols from the reaction products in the oxidative nitration of p-xylene at 28° and acetoxymercuri-p-xylene at 20-50° and of m-xylene, carried out by Kholevo and Éitingon at the boiling point and at 75° [4].

Treatment of p-xylene at 3-5° with a mixture of mercury nitrate and nitric acid of medium concentration in the presence of acetic acid and ligroin, added to lower the freezing point of the p-xylene, yielded the x,x-dinitro-2-hydroxy-p-xylene mentioned above. The identity of the latter with 3,5-dinitro-2-hydroxy-p-xylene was demonstrated by its synthesis by nitration of p-xylenol and 5-nitro-2-hydroxy-p-xylene.

However, the problem of whether the dinitro-p-xylenol was formed through p-hydroxy-p-xylylhydroxylamine and 5-nitroso-2-hydroxy-p-xylene or through p-xylyldiazonium nitrate remained unsolved. This problem could be solved by a tracer method, for example.

EXPERIMENTAL

Acetoxymercuri-p-xylene. A mixture of 318.5 g of p-xylene and 63.7 g of mercury acetate was heated to boiling over a period of 50 minutes under reflux and with stirring, then boiled for 5 minutes and gradually cooled to 25° over 1 hour. After removal of the precipitate of polymercurated compounds (9.5 g) by filtration and the p-xylene by steam distillation, the residue in the flask was diluted with water, cooled in ice and filtered. We obtained 57.1 g of acetoxymercuri-p-xylene (78.3% calculated on mercury) with m.p. 112-113°. The fine, colorless crystals (from dilute acetic acid) had m.p. 114.2-114.7°.

Found %: C 32.52, 32.35; H 3.19, 3.10; Hg 55.0, 55.06. $C_{10}H_{12}O_2Hg$. Calculated %: C 32.92; H 3.22; Hg 54.99.

The product was soluble in alcohol, acetic acid, acetone and benzene and less so in water.

Chloromercuri-p-xylene. This product was obtained by treating a solution of acetoxymercuri-p-xylene in p-xylene with a saturated solution of sodium chloride.

The colorless needles (from benzene and alcohol) had m.p. 184.8-185.5°; a mixture of this with chloromercuri-p-xylene (m.p. 186.2-186.5°), obtained from pure p-xylidine by the diazo method [5], had m.p. 186.0-186.5°. 63.1 g of p-xylidine hydrochloride, 120 ml of concentrated hydrochloric acid, 120 g of ice, 32.3 g of sodium nitrite and 110 g of mercuric chloride in 110 ml of concentrated hydrochloric acid and 120 g of ice gave, by the diazo method, 117.6 g (66.8%) of the binary salt of p-xylyldiazonium chloride and mercuric chloride.

Found %: N 5.95. $C_8H_9N_2Cl_3Hg$. Calculated %: N 6.37.

The light, crystalline substance with a yellowish tinge was sparingly soluble in water, alcohol and benzene, more so in acetone and insoluble in ether; it was unstable during storage. In one experiment the salt decomposed explosively while it was being dried in air at 31°.

115.4 g of the binary salt and 60 g of freshly prepared copper powder in 650 ml of acetone at 15-8° gave (extraction with acetone and recrystallization from benzene) 46.2 g (51.6%) of chloromercuri-p-xylene with m.p. 186.2-186.5°.

Found %: C 27.86, 27.92; H 2.64, 2.70; Cl 10.22. C_8H_9ClHg. Calculated %: C 28.16; H 2.66; Cl 10.39.

The product was difficultly soluble in alcohol and benzene, more so in glacial acetic acid and acetone and insoluble in ether.

p-Xylylmercury Nitrate. This substance was obtained by the action of an alcohol solution of 1.98 g of silver nitrate on an alcohol-acetone solution of 3.98 g of chloromercury-p-xylene in a yield of 3.7 g (86.4%). The colorless crystals had m.p. 163.5-164° (decomp.).

Found %: C 26.10, 25.91; H 2.58, 2.72; N 3.80, 3.72. $C_8H_9O_3NHg$. Calculated %: C 26.13; H 2.47; N 3.81.

The substance darkened and became infusible during storage, especially in light.

Bis-2,5-dimethylphenylmercury. This substance was obtained in 91% yield of symmetrization of chloromercuri-p-xylene with copper in the presence of ammonia similarly to mercuri-bis-p-(methyl benzoate) [6].

The colorless needles had m.p. 127.5-128° (from alcohol).

Found %: C 47.11, 47.02; H 4.45, 4.43. $C_{16}H_{18}Hg$. Calculated %: C 46.75; H 4.38.

According to literature data, bis-2,5-dimethylphenylmercury obtained from 2,5-dimethylbromobenzene by the action of sodium amalgam and ethyl chloroformate melted at 123° [7].

Oxidative Nitration of Acetoxymercuri-p-xylene. 4 g of acetoxymercuri-p-xylene was gradually added over a period of 1 hour with vigorous stirring to 28 ml of 58% nitric acid at 2-3°. The mixture was then stirred for 5 hours at 2-4°. To form nitrogen oxides during the addition and stirring period, 1.5 g of sodium nitrate was gradually added. The yellow precipitate was collected, washed with ice water and dried. Its weight was 1.84 g. The precipitate was extracted with ether. The ether solution was stirred with a 10% solution of sodium bicarbonate. Acidification of the bicarbonate solution yielded 0.55 g of dinitro-p-xylenol with m.p. 118.5-119.5° (23.8%).

The light-yellow platelets had m.p. 121.2-122° (from water); a mixture with x,x-dinitro-2-hydroxy-p-xylene, obtained from p-xylenol by sulfonation and subsequent nitration [4] or by direct nitration with fuming nitric acid in glacial acetic acid, had m.p. 121-122°.

Found %: N 13.08, 13.12. $C_8H_8O_5N_2$. Calculated %: N 13.21.

An identical dinitro-2-hydroxy-p-xylene was obtained by nitration of 5-nitro-2-hydroxy-p-xylene with nitric acid in acetic acid solution. The latter was obtained by nitration of p-xylenol [8], synthesized from pure p-xylidine [9].

Oxidative Nitration of p-Xylene. 80 g of p-xylene was added at -1-3° with mechanical stirring over a period of 5 hours to a mixture of 353 ml of 58% nitric acid, 82.5 g of mercury nitrate, 10 ml of glacial acetic acid and 100 ml of ligroin. The mixture was then stirred for 6 hours 30 minutes at -3-7°. During the addition and the stirring period, 2 g of sodium nitrite was gradually added to the reaction mixture.

After the stirring period the organic layer was separated from the acid layer, washed with ice-water and stirred with 10% sodium carbonate solution. Acidification of the sodium carbonate solution yielded 0.2 g of a substance with m.p. 117.5-119.5°.

After recrystallization from ligroin, the substance melted at 121-121.4° and did not depress the melting point of 3,5-dinitro-2-hydroxy-p-xylene, obtained by nitration of p-xylenol.

Found %: N 13.21, 13.10. $C_8H_8O_5N_2$. Calculated %: N 13.21.

SUMMARY

1. The action of 58% nitric acid containing oxides of nitrogen on acetoxymercuri-p-xylene at low temperature yielded x,x-dinitro-2-hydroxy-p-xylene. It was shown that the structure of the latter corresponded to 3,5-dinitro-2-hydroxy-p-xylene.

2. The oxidative nitrating effect of mercury nitrate in the nitration of p-xylene with 58% nitric acid at low temperature was demonstrated.

3. Acetoxymercuri-p-xylene, the binary salt of p-xylyldiazonium chloride and mercuric chloride, chloromercuri-p-xylene and p-xylylmercury nitrate were synthesized and described.

We would like to thank S. V. Bogdanov for directing the work.

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SOME REACTIONS OF β,β'-DIHYDROXYDIETHYLAMINO-p-BENZOQUINONE

A. Ya. Berlin

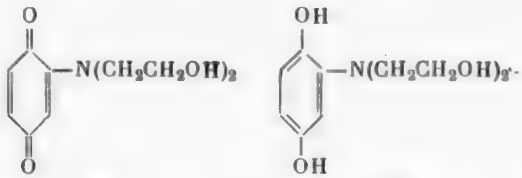
Institute of Experimental Pathology and Cancer Therapy
Academy of Medical Sciences USSR Moscow

The condensation of p-benzoquinone with amines normally yields the corresponding derivatives of 2,5-diaminoquinone [1]; on the other hand, the formation of monoamines has only been observed in individual cases and under special conditions [2]. By the reaction of p-benzoquinone with diethanolamine in an alcohol-ether solution we obtained only β,β'-dihydroxydiethylamino-p-benzoquinone (I) in more than 90% yield. A second diethanolamino group was not introduced into the benzoquinone nucleus, apparently due to the practically complete precipitation of the monoamino derivative.

The dihydroxydiethylaminoquinone (I) was a brownish yellow, crystalline substance with certain peculiarities: when heated with water or alcohol it slowly dissolved with an intense cherry-red color, which gradually disappeared on cooling with the simultaneous separation of the starting material in a crystalline state. Treatment with mineral acids rapidly produced a dark-violet color, very reminiscent of the color of permanganate solution.

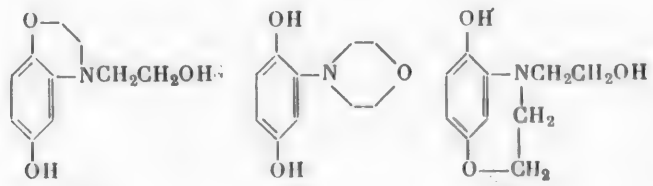
A brief communication [3] appeared in the literature very recently on an analogous synthesis of β,β'-dihydroxydiethylamino-benzoquinone and certain compounds similar to it.

Interesting results were obtained on attempting to reduce (I) to the corresponding hydroquinone (II) under certain conditions.



(I) (II)

The action of zinc dust on a solution of (I) in 8-10% acetic acid formed a colorless substance with m.p. 106-107°, which had the composition $C_{10}H_{13}O_3N$ according to analysis results and a molecular weight determination. Of the three possible structural formulas corresponding to this composition, the most probable one was undoubtedly the formula of 4-β-hydroxyethyl-6-hydroxybenzomorpholine (III).

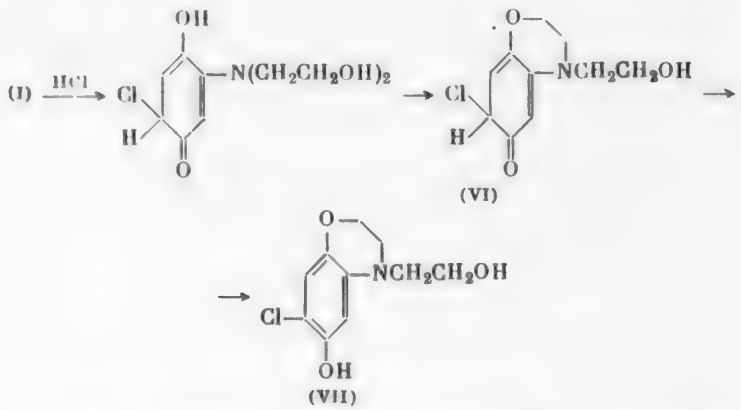


(III) (IV) (V)

The other two formulas can hardly be considered. Actually it is known that the formation of a morpholine ring from diethanolamine derivatives, as in (IV), usually proceeds under much more drastic conditions [4] and in the case of (V), the possibility of ready cyclization into a seven-membered ring, condensed with a benzene nucleus in positions 1 and 3, should also be considered extremely improbable.

Apparently the molecule of the hydroquinone derivative (II) formed by the reduction underwent quite rapid intramolecular elimination of the elements of water from the alcoholic hydroxyl of the hydroxyethyl group and the phenolic hydroxyl in a position ortho to the amino group.

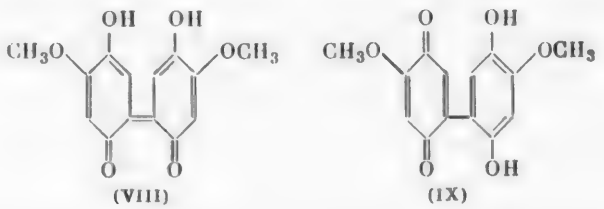
Different results were obtained on reducing the dark-violet solution of quinone (I) in 2-3% hydrochloric acid with zinc dust or SO_2. In this case we isolated two bases and separated them by means of their different solubilities in dilute (1 : 1) hydrochloric acid. One of these bases, (m.p. 94-95°) whose hydrochloride was difficultly soluble in dilute hydrochloric acid, contained chlorine, had the composition $C_{10}H_{12}O_3NCl$ and was the product of cyclization with elimination of water from the monochloro derivative of dihydroxydiethylaminohydroquinone. As it was undoubtedly 4-β-hydroxyethyl-6-hydroxy-7-chlorobenzomorpholine (VII), this compound could have been formed by the addition of the elements of HCl to the original quinone (I) and subsequent closure of the morpholine ring by the scheme



Consequently zinc dust did not act as a reducing agent in this case. Actually, in another experiment the action of hydrochloric acid alone on (I) yielded the same compound (VII).

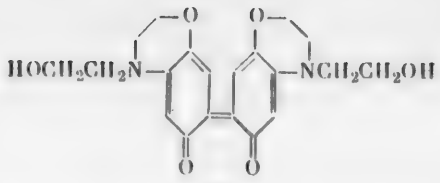
The second base (m.p. 177-178° with decomp.), whose hydrochloride was soluble in dilute hydrochloric acid, did not contain chlorine and had the composition $C_{20}H_{24}O_6N_2$.

Dimerization of certain substituted quinones under the action of mineral acids has been described in a series of investigations [5-8]. Thus, methoxy-p-benzoquinone yielded a substance to which Erdtman [7] ascribed the structure (VIII) or (IX).

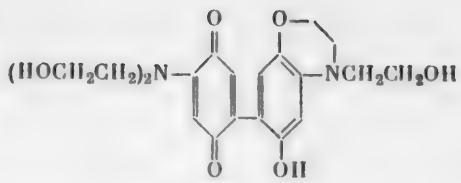


Ioffe and Sukhina [8] were inclined to consider this compound as the intramolecular quinhydrone (IX).

In our case also both types of compound, (X) and (XI), were possible.

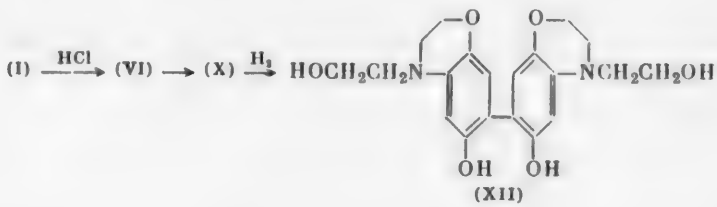


(X)



(XI)

However, it seemed to us that the most probable structure was the symmetrical one (X), which contains an indigoid system of bonds responsible for the intense dark-violet color of the solution formed from (I) and a mineral acid. The reduction of such solutions of both (X) and (XI) should ultimately give colorless 7,7'-bis-(4-β-hydroxyethyl-6-hydroxybenzomorpholine) (XII), which we isolated as a substance with m.p. 177-178°. The formation of dimer (XII) may be illustrated by the following scheme.



(XII)

Diphenol (XII) was converted by oxidation into diketone (X), but it was impossible to isolate directly either (X), (XI) or the original quinone (I) from the dark-violet acid solution.

The diacetate of (VII) and the tetraacetate of (XII) were obtained in the same way.

EXPERIMENTAL*

β,β'-Dihydroxydiethylamino-p-benzoquinone (I). A solution of 5 g of diethanolamine in 50 ml of alcohol was gradually added with stirring to a solution of 11 g of p-benzoquinone in 300 ml of ether. A light-brown precipitate began to separate immediately and this was collected the next day and washed carefully with ether. The yield was 9.37 g (93%). Recrystallization from 500 ml of alcohol yielded brownish yellow, needlelike crystals. The substance began to darken at 156° and decomposed with the evolution of gas at 161°.

Found %: C 56.97, 56.92; H 6.34, 6.37; N 6.82, 6.89. $C_{10}H_{13}O_4N$. Calculated %: C 56.92; H 6.21; N 6.64.

During recrystallization from alcohol or water, the hot solution acquired a cherry red color, which paled and changed to dark-yellow when the solution cooled and crystals separated. When treated with mineral acids the substance formed a dark-violet solution.

4-β-Hydroxyethyl-6-hydroxybenzomorpholine (III). A little zinc dust was added to a solution of 2 g of quinone (I) in 100 ml of 8-10% acetic acid. On stirring, the red solution rapidly became pale yellow. After neutralization with an aqueous solution of ammonia, the substance was extracted with ethyl acetate and the solution obtained was dried with anhydrous Na_2SO_4. The solvent was removed and the residue (0.98 g) recrystallized from benzene. The colorless crystals had m.p. 106-107°.

Found %: C 61.39, 61.11; H 6.78, 6.79; N 7.06, 7.01; act. H 1.05, 1.02. M 215, 212. $C_{10}H_{13}O_3N$. Calculated %: C 61.54; H 6.67; N 7.18; act. H 1.03. M 195.

The somewhat high results for the molecular weight determination (by Rast's method) were probably caused by some association due to the presence of free hydroxyl groups in the molecule.

Action of Zinc Dust on a Solution of Dihydroxydiethylamino-p-benzoquinone in Hydrochloric Acid. 4-β-Hydroxyethyl-6-hydroxy-7-chlorobenzomorpholine (VII) and 7,7'-bis-(4-β-hydroxyethyl-6-hydroxybenzomorpholine) (XII). Zinc dust was gradually added with stirring to a solution of 2 g of quinone (I) in a mixture of 5 ml of concentrated hydrochloric acid and 100 ml of water until the dark-violet color of the solution changed to a dirty yellow. After neutralization of the solution with an amount of CH_3COONa equivalent to the hydrochloric

*All the melting points are corrected.

acid taken, the reaction product was extracted with ethyl acetate. The solvent was removed and the yellowish brown residue, which slowly crystallized, was treated with 25 ml of dilute (1 : 1) hydrochloric acid.

The insoluble residue of the hydrochloride was collected, washed with a small amount of dilute hydrochloric acid and dried. The greenish crystals, which acquired a violet color in air, had m.p. 145-155° (with decomp.). The weight was 0.56 g. Treatment of the hydrochloride with an aqueous $NaHCO_3$ solution yielded the base (VII), which was recrystallized from benzene. The colorless crystals with a brownish violet tint had m.p. 94-95° (with decomp.).

Found %: C 52.40, 52.35; H 5.39, 5.48; N 6.48, 6.24; Cl 15.61, 15.66. $C_{10}H_{12}O_3NCl$. Calculated %: C 52.29; H 5.27; N 6.10; Cl 15.43.

The hydrochloric acid filtrate after separation of hydrochloride of (VII) was evaporated to dryness. The residual dark, crystalline substance was ground with n-butanol containing a few drops of conc. HCl and separated. We obtained 0.67 g of dark-grey hydrochloride of (XII), which was purified by solution in 4 ml of conc. HCl and precipitation with 7 ml of methanol. The light-grey crystals had m.p. 204° (with decomp.).

Found %: C 51.74, 51.76; H 5.95, 6.18; N 5.70, 5.50; Cl 15.13, 14.94. $C_{20}H_{26}O_6N_2Cl_2$. Calculated %: C 52.06; H 5.69; N 6.07; Cl 15.38.

The action of aqueous $NaHCO_3$ solution on a solution of the hydrochloride with m.p. 204° yielded the base (XII), which was recrystallized from methanol. The colorless crystals with a light-green tinge had m.p. 177-178° with decomp. with the capillary inserted at 170°.

Found %: C 61.64, 61.64; H 6.26, 6.20; N 6.95, 6.81. $C_{20}H_{24}O_6N_2$. Calculated %: C 61.91; H 6.20; N 7.22.

The same results were obtained by the action of SO_2, sodium sulfite or hydrosulfite.

Action of Hydrochloric Acid on Quinone (I). To 1 g of quinone (I) was added 2-3 ml of concentrated hydrochloric acid. Heat was evolved and a black-violet solution formed and rapidly crystallized. The precipitate was collected and washed with alcohol and concentrated hydrochloric acid. The light-violet crystals had m.p. 145-155° (with decomp.) and did not depress the melting point of the hydrochloride of (VII).

After neutralization with CH_3COONa solution, the filtrate deposited a viscous black mass and the solution became red with a brownish fluorescence. No individual substance could be isolated from the precipitate.

7,7'-Dehydro-7,7'-bis-(6,7-dihydro-4-β-hydroxyethyl-6-hydroxybenzomorpholine (X). To a solution of 0.2 g of base (XII) in 15 ml of alcohol was added a solution of 0.11 g of p-benzoquinone in 7 ml of ether. A dark-brown precipitate formed, which was collected, washed with ether and recrystallized from a large amount of alcohol. The needlelike crystals (under a microscope) were black-violet in reflected light and dark brown in transmitted. They did not melt up to 320°. The weight was 15 mg.

Found %: C 62.42; H 6.00. $C_{20}H_{22}O_6N_2$. Calculated %: C 62.23; H 5.75.

4-β-Acetoxyethyl-6-acetoxy-7-chlorobenzomorpholine. To a solution of 0.49 g of base (VII) in 10 ml of anhydrous pyridine was added 2 ml of acetic anhydride. The next day the liquid was poured into 100 ml of water, the precipitated oil extracted with ether and the ether solution dried with anhydrous Na_2SO_4. After removal of the ether, the residue crystallized and was recrystallized from ligroin (50-60°). The weight was 0.32 g and the m.p. 71-71.5°.

Found %: C 53.87, 53.72; H 5.19, 5.41; N 4.22, 4.24. M 322. $C_{14}H_{16}O_5NCl$. Calculated %: C 53.60; H 5.14; N 4.46. M 313.7.

7,7'-Bis-(4-β-acetoxyethyl-6-acetoxybenzomorpholine). The acetylation of 0.21 g of base (XII) was carried out similarly to that described above. We obtained 0.28 g of tetraacetate, which was recrystallized from ethyl acetate and from alcohol. The m.p. was 196-197°.

Found %: C 60.17, 60.11; H 5.79, 5.80; N 5.28, 5.34. M 522, 569. $C_{28}H_{32}O_{10}N_2$. Calculated %: C 60.43; H 5.80; N 5.04. M 556.

SUMMARY

1. β,β'-Dihydroxydiethylamino-p-benzoquinone was synthesized from p-benzoquinone and diethanolamine.

2. The dihydroxyquinone was converted into 4-β-hydroxyethyl-6-hydroxybenzomorpholine by reduction in a weakly acid medium.

3. The action of hydrochloric acid on the dihydroxyquinone formed 4-β-hydroxyethyl-6-hydroxy-7-chlorobenzomorpholine and reduction of the hydrochloric acid solution yielded 7,7'-bis-(4-β-hydroxyethyl-6-hydroxybenzomorpholine).

4. A possible mechanism for these reactions was considered.

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A CONTRIBUTION ON THE CATALYTIC HALOGENATION OF PHENYLTRICHLOROSILANE

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In a series of papers published previously on the halogenation of aromatic silanes in the presence of a catalyst, we reported [1-4] that the $SiCl_3$ group was a meta-directing substituent by nature, but according to our observations the trichlorosilyl group behaved anomalously in these reactions and directed into the ortho- and para-positions.

A. D. Petrov, M. I. Batuev et al. [5] repeated our experiments on the bromination of phenyltrichlorosilane in the presence of iron and found that o-bromophenyltrichlorosilane was formed in this reaction besides the para-derivative (content of ortho- and para-derivatives, 69%). They obtained different results in the chlorination of phenyltrichlorosilane. In this case the main reaction product was not p- but m-chlorophenyltrichlorosilane (content of meta-isomer, 74%). These authors used IR-spectral analysis to determine the composition of the reaction products.

We arrived at our conclusions on the structure and composition of the chlorination and bromination products of phenyltrichlorosilane from the results of a chemical investigation of their degradation products obtained by a method analogous to that of Kipping and Cusa [6]. The latter consisted of treating the substituted aromatic silane under test with a mixture of bromine and water at 140-170°, which ruptured the C-Si bond to form the corresponding substituted aryl bromide. However, a detailed check of the applicability of this method to substituted arylchlorosilanes showed that it led to distorted results. In actual fact, the action of bromine water on both p-chlorophenyltrichlorosilane (as was established previously) and on m-chlorophenyltrichlorosilane (the two isomers were obtained from the appropriate chlorophenylmagnesium bromides and $SiCl_4$) formed only p-chlorobromobenzene (60.4 and 34.6% yields, respectively). These experiments showed that the formation of chlorobromobenzenes occurred not as a result of rupture of the C-Si bond by bromine but as a result of bromination of chlorobenzene. It was shown previously [7] that a mixture of bromine and chlorophenylchlorosilane did not interact at 150-200°. By subsequent experiments we established that at 140-200° 40% hydrobromic acid was capable of rupturing the C-Si bond in phenyltrichlorosilane and monochlorophenyltrichlorosilane with the formation of benzene (60.6% yield) and chlorobenzene (27.4% yield), respectively.

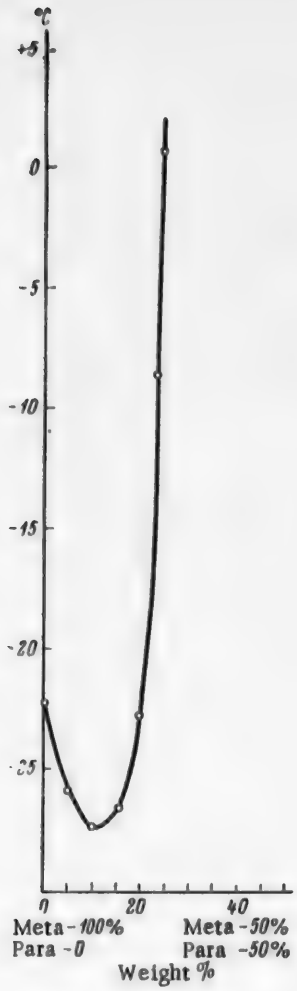
This readily explains the formation of p-chlorobromobenzene by degradation of both p- and m-chlorophenyltrichlorosilanes with bromine water, which evidently occurred under the action of hydrobromic acid, produced by hydrolysis of the bromine by water, and bromine reacting with the chlorobenzene thus obtained.

In connection with what has been said, a need arose for a different method for determining the structure of chloro and bromo derivatives of phenyltrichlorosilane. Benkeser and Torkelson [8] found that phenyltrimethylsilane was degraded by bromine even under normal conditions by the scheme

$$C_6H_5Si(CH_3)_3 + Br_2 \rightarrow C_6H_5Br + (CH_3)_3SiBr.$$

We showed that p- and m-chlorophenyltrimethylsilane behaved analogously and gave high yields of p-chlorobromo- and m-chlorobromobenzenes, respectively, and trimethylbromosilane.

In the chlorination of phenyltrichlorosilane in the presence of iron to the monochloro derivative, the reaction products yielded two fractions corresponding to monochlorophenyltrichlorosilane in analysis: one with b.p. 98-107° at 11 mm and the other with b.p. 108.5-112° at 11 mm. Bromine degradation of chlorophenyltrimethyl-



Melting point diagram of mixtures of p- and m-chlorobromobenzenes.

silane, obtained by exhaustive methylation (with CH_3MgI) of the low-boiling fraction of monochlorophenyltrichlorosilane, yielded chlorobromobenzene [together with $(CH_3)_3SiBr$] in the form of a liquid, crystallizing at -26°. As shown by comparison with the melting point diagram we obtained for mixtures of p- and m-chlorobromobenzenes (see figure), the freezing point of the mixture of chlorobromobenzenes obtained (-26°) was close to the freezing point (-25.7°) of a mixture with 95% of the meta- and 5% of the para-isomer. Spectral (IR) analysis of this mixture indicated the same composition.

Bromine degradation of the methylated high-boiling fraction of chlorophenyltrichlorosilane, corresponding in constants to o-chlorophenyltrichlorosilane [5], yielded o-chlorobromobenzene, which confirmed that this substance had the structure of o-chlorophenyltrichlorosilane.

From the data described above and presented in the experimental section, it follows that the chlorination of phenyltrichlorosilane in the presence of $FeCl_3$ proceeds with the formation of a mixture of m-, o- and p-chlorophenyltrichlorosilanes in the ratio 75:21:4, which agrees well with the data in [5].

If an analogous degradation was carried out on the main fraction of products from the catalytic (iron) bromination of phenyltrichlorosilane, corresponding to monobromophenyltrichlorosilane, in composition (after preliminary methylation), it was possible to isolate p-dibromobenzene (40.4% of the total weight of the mixture of dibromobenzenes obtained) and o-dibromobenzene (25.1%), from which it follows (see also experimental section) that in the bromination of phenyltrichlorosilane at least 68% of the mixture of bromophenyltrichlorosilanes formed consisted of the para- (37%) and ortho-isomers (31%).

These data once again confirm that in this reaction the $SiCl_3$ group behaves anomalously as an ortho – para directing group. At the same time, the above indicates that a series of our previous conclusions on the structure of chlorination products of arylchlorosilanes [3, 4, 9] requires modification.

EXPERIMENTAL

1. Chlorination of phenyltrichlorosilane was carried out in a glass column (220 mm high and 25 mm diameter), fitted with a reflux condenser, a bubbler (porous glass plate) for the input of chlorine and a thermometer.

Gaseous chlorine was passed into a mixture of 90 g of phenyltrichlorosilane and 1.5 g of anhydrous $FeCl_3$ at 50-60° until the increase in weight reached 12.7 g. Vacuum distillation of the crude mixture gave 95 g of reaction products, boiling over the range 78-120° at 11 mm. Vacuum distillation of these products (11 mm) from a flask with a pear fractionating column (400 mm long) gave fractions:

1st, b.p. 78-80°, 12.7 g of unreacted $C_6H_5SiCl_3$; 2nd, b.p. 81-95°, 8.2 g; 3rd, b.p. 98-107°, d_{20}^{20} 1.4414, $n^{20}D$ 1.5430, 52.4 g.

Found %: Cl (total) 57.3, 57.1; Cl (hydrolyzable) 43.2, 43.8. $C_6H_4ClSiCl_3$. Calculated %: Cl (total) 57.72; Cl (hydrolyzable) 43.29.

4th, b.p. 108.5-112°, d_{20}^{20} 1.4620, $n^{20}D$ 1.5500, 14.2 g.

Found %: Cl (total) 57.4, 57.5; Cl (hydrolyzable) 43.6, 43.9. $C_6H_4ClSiCl_3$. Calculated %: Cl (total) 57.72; Cl (hydrolyzable) 43.29.

5th, b.p. 110-120°, d_{20}^{20} 1.5066, $n^{20}D$ 1.5549, 3.3 g.

Found %: Cl (total) 60.8, 61.3; Cl (hydrolyzable) 40.1, 40.4. $C_6H_4ClSiCl_3$. Calculated %: Cl (total) 57.72; Cl (hydrolyzable) 43.29. $C_6H_3Cl_2SiCl_3$. Calculated %: Cl (total) 63.28; Cl (hydrolyzable) 37.97.

Part of the main fraction (3rd), which was a monochloro derivative, was converted into $ClC_6H_4Si(CH_3)_3$. A solution of 20 g of the monochloride (3rd fraction) in 50 ml of ether was added dropwise with cooling to an ether solution of CH_3MgI, prepared from 6.8 g of magnesium, 37.4 g of methyl iodide and 100 ml of absolute ether.

After the addition, the reaction mixture was boiled for 30 minutes, cooled and decomposed with 10% hydrochloric acid. From the ether layer we isolated 13 g (86.6%) of a liquid with b.p. 65-69° at 6 mm, 78-81° at 9 mm, d_{20}^{20} 1.0144, $n^{20}D$ 1.5110.

Found %: Cl 19.01, 19.42. $ClC_6H_4Si(CH_3)_3$. Calculated %: Cl 19.24.

Similarly, treatment of 4 g of the 4th fraction (b.p. 108.5-112° at 11 mm) with CH_3MgI (from 1.4 g of magnesium and 7.5 g of methyl iodide) gave 2.2 g of $ClC_6H_4Si(CH_3)_3$ (73.3% yield) with b.p. 85-86° at 12 mm, d_{20}^{20} 1.0453, $n^{20}D$ 1.5175.

Found %: Cl 19.52, 19.61. $ClC_6H_4Si(CH_3)_3$. Calculated %: Cl 19.24.

2. Bromination of phenyltrichlorosilane was carried out in a glass column (220 mm high and 25 mm diameter), fitted with a reflux condenser, a dropping funnel for the addition of bromine and a thermometer.

Over a period of 1.5 hours, 50 g of dry bromine was added to a mixture of 72 g of phenyltrichlorosilane and 0.4 g of metallic iron powder at 50-55°. Vacuum distillation of the crude mixture yielded 91 g of reaction products, boiling in the range 78-120° at 10 mm. Vacuum distillation (11 mm) of these from a flask with a pear fractionating column (400 mm high) yielded fractions:

1st, b.p. 78-81°, 16.0 g of unreacted $C_6H_5SiCl_3$; 2nd, b.p. 82-112°, 12.1 g; 3rd, b.p. 113-117°, d_{20}^{20} 1.6764, $n^{20}D$ 1.5660, 53.1 g.

Found %: Br 38.1, 38.4; Cl (hydrolyzable) 36.2, 36.4. $C_6H_4BrSiO_{1.5}$. Calculated %: Br 38.4. $C_6H_4BrSiCl_3$. Calculated %: Cl (hydrolyzable) 36.6. 4th, b.p. 118-120°, d_{20}^{20} 1.6968, $n^{20}D$ 1.5700, 4.8 g.

Found %: Br 38.0, 38.1; Cl (hydrolyzable) 36.1, 36.0. $C_6H_4BrSiO_{1.5}$. Calculated %: Br 38.4. $C_6H_4BrSiCl_3$. Calculated %: Cl (hydrolyzable) 36.6.

As described above for the monochloro derivative, part of the main fraction (3rd), which was the monobromo derivative, was converted into $BrC_6H_4Si(CH_3)_3$. The reaction of 20 g of $BrC_6H_3SiCl_3$ (3rd fraction) with CH_3MgI, prepared from 5.8 g of magnesium and 31.8 g of methyl iodide in dry ether (150 ml), yielded 12.5 g (80.5%) of a liquid.

B.p. 93-94° at 10 mm, d_{20}^{20} 1.2288, $n^{20}D$ 1.5325.

Found %: Br 35.1, 35.3. $BrC_6H_4Si(CH_3)_3$. Calculated %: Br 34.93.

According to data in [10]: b.p. 146-148° at 50 mm, d_4^{20} 1.2197, $n^{20}D$ 1.5302.

3. p-Chlorophenyltrichlorosilane was obtained from 50 g of p-chlorobromobenzene, 6.6 g of magnesium and 47.6 g of $SiCl_4$ in an absolute ether medium under the conditions described previously [11, 12]. We isolated 16.6 g (25.8%) of a liquid.

B.p. 100-102° at 11 mm, d_4^{20} 1.4330, $n^{20}D$ 1.5422; according to data in [12]: b.p. 100° at 11 mm, d_4^{20} 1.4316, $n^{20}D$ 1.5418.

p-Chlorophenyltrimethylsilane was obtained by the method described above by reacting CH_3MgI, prepared from 2.7 g of magnesium and 15 g of methyl iodide, with 8 g of $p\text{-}ClC_6H_4SiCl_3$ in absolute ether (110 ml). We isolated 4 g (66.6%) of a liquid.

B.p. 85-86° at 9 mm, d_4^{20} 1.0012, $n^{20}D$ 1.5090. According to data in [13]: d_4^{20} 1.0002, $n^{20}D$ 1.5090; according to data in [10]: b.p. 119-120° at 50 mm d_4^{20} 1.0282, $n^{20}D$ 1.5128.

4. m-Chlorophenyltrichlorosilane was obtained under conditions analogous to those for the preparation of the para-isomer from 50 g of m-chlorobromobenzene (the latter was synthesized from $m\text{-}BrC_6H_4NH_2$ through the diazo compound). We obtained 18.3 g (28.5%) of a liquid.

B.p. 95-97° at 11 mm, d_4^{20} 1.5424. According to data in [12]: b.p. 230.5° at 738 mm, d_4^{20} 1.4384, $n^{20}D$ 1.5421.

m-Chlorophenyltrimethylsilane was obtained as described above from 15 g of methyl iodide, 2.7 g of magnesium and 8 g of m-$ClC_6H_4SiCl_3$ in an absolute ether medium (120 ml). We obtained 4.7 g (78.3%) of a liquid with b.p. 84-85° at 9 mm, d_4^{20} 1.0071, $n^{20}D$ 1.5108.

5. Degradation of Monochlorophenyltrichlorosilanes with Bromine Water in a Sealed Tube. a) Degradation of p-$ClC_6H_4SiCl_3$. Into two glass tubes were placed 3.4 g of p-$ClC_6H_4SiCl_3$, 0.8 ml of bromine and 4 ml of water. The sealed tubes were heated at 170-180° for 8 hours. The cooled tubes were opened and their contents combined, neutralized with 10% sodium carbonate solution and extracted with ether. After steam distillation, the ether solution yielded 1.5 g of a crystalline substance with m.p. 66.1° (from alcohol, which was p-chlorobromobenzene. The yield was 60.4%.

b) Degradation of m-$ClC_6H_4SiCl_3$. When a mixture of 3.2 g of m-$ClC_6H_4SiCl_3$, 0.8 ml of bromine and 4 ml of water was heated under analogous conditions, the reaction products yielded 0.8 g (34.6%) of p-chlorobromobenzene with m.p. 65.7°.

c) Degradation of $ClC_6H_4SiCl_3$, Obtained by Chlorination of $C_6H_5SiCl_3$ in the Presence of $FeCl_3$. Heating a mixture of 6 g of monochlorophenyltrichlorosilane, obtained by chlorination of $C_6H_5SiCl_3$ in the presence of $FeCl_3$ (3rd fraction, see exp. 1), 1.5 ml of bromine and 6 ml of water under analogous conditions (in three tubes) led to the formation of 2.4 g (53.3%) of p-chlorobromobenzene with m.p. 65.2°.

In the last two cases, together with p-ClC_6H_4Br a tar was formed which approximately corresponded to the composition $(C_6H_4ClSiO_{1.5})_n$ according to the chlorine content.

Found %: Cl 20.3, 20.1. $(C_6H_4ClSiO_{1.5})_n$. Calculated %: Cl 21.7.

6. Degradation of Phenylchlorosilanes with 40% Hydrobromic Acid in a Sealed Tube. a) Degradation of $C_6H_5SiCl_3$. Into a glass tube was placed 1.8 g of $C_6H_5SiCl_3$ and 2.5 ml of 40% hydrobromic acid. The sealed tube was heated at 170-200° for 12 hours. Subsequent processing was as in the degradation with bromine water. The ether solution yielded 0.4 g (60.6%) of benzene with b.p. 78-80°. For identification, the latter was nitrated to m-dinitrobenzene with m.p. 89.3° (from alcohol).

b) Degradation of $ClC_6H_4SiCl_3$, Obtained by Chlorination of $C_6H_5SiCl_3$ in the Presence of $FeCl_3$. When a mixture of 6 g of monochlorophenyltrichlorosilane, obtained by chlorination of $C_6H_5SiCl_3$ in the presence of $FeCl_3$ (3rd fraction, see exp. 1). and 7.5 ml of 40% hydrobromic acid was heated under analogous conditions (in three tubes), the reaction products yielded 0.74 g (27.4%) of chlorobenzene. The main product of the reaction was a chlorine-containing organosilicon resin.

7. Degradation of Monochloro(bromo)phenyltrimethylsilanes with Bromine. a) Degradation of p-$ClC_6H_4Si(CH_3)_3$. Over a period of 10 minutes, 3.7 g of bromine was added dropwise with stirring to 3.9 g of p-$ClC_6H_4Si(CH_3)_3$. Since the reaction involved appreciable heat evolution (the temperature of the mixture rose to 70-80°), the bromine was added with cooling (25-30°). When all the bromine had been added, the mixture was heated at 60-70° for 20 minutes and the $(CH_3)_3SiBr$ (2.4 g, 75% yield) with b.p. 79-80° distilled from the mixture. The residue after distillation of the $(CH_3)_3SiBr$ crystallized on cooling.

Vacuum distillation (10 mm) of this yielded 3.1 g (77.5%) of p-chlorobromobenzene with m.p. 66.2°.

b) Degradation of m-$ClC_6H_4Si(CH_3)_3$. Similarly, from 4 g of m-$C_6H_4Si(CH_3)_3$ and 3.8 g of bromine we obtained 2.5 g (78.1%) of $(CH_3)_3SiBr$ and 3.4 g (85%) of m-chlorobromobenzene with b.p. 67-68° at 10 mm, d_4^{20} 1.6923, $n^{15}D$ 1.5784.

Degradation of Chlorophenyltrimethylsilanes Obtained from Monochlorophenyltrichlorosilanes Isolated in the Chlorination of $C_6H_5SiCl_3$ in the Presence of $FeCl_3$. Degradation of Trimethyl Derivative of the Fraction with b.p. 98-107° at 11 mm. The reaction of 11.5 g of the monochlorophenyltrimethylsilane and 10.8 g of bromine under analogous conditions yielded 8.5 g (89.4%) of $(CH_3)_3SiBr$ and 10.4 g (87.4%) of a colorless liquid corresponding to chlorobromobenzene in analysis and crystallizing at -26°.

B.p. 67-70° at 10 mm, d_{20}^{20} 1.6292, $n^{20}D$ 1.5770. According to data in [14]: for p-ClC_6H_4Br m.p. 64.6°; for o-ClC_6H_4Br f.p. -12.6°, d_4^{20} 1.6444, $n^{17.3}D$ 1.5821; for m-ClC_6H_4Br f.p. -21.2°, d_4^{20} 1.6297, $n^{17.1}D$ 1.5773.

ClC_6H_4Br content of mixture (in g)		(in %)		Freezing point
m-	p-	m-	p-	
5.40	—	100	—	—22.2°
5.40	0.28	95	5	—25.7
5.40	0.60	90	10	—27.4
5.40	0.95	85	15	—26.5
5.40	1.35	80	20	—22.7
5.40	1.80	75	25	— 8.6
5.40	2.31	70	30	+ 0.8
5.40	2.90	65	35	+ 9.6
5.40	3.60	60	40	+16.6

Mixture isolated from experiment —26.0

In order to determine the qualitative and quantitative composition of the mixture of chlorobromobenzenes obtained, we used the data from its thermal analysis, obtained by a generally accepted procedure [15]. The results of these determinations are presented in the table and the figure.

From the fact that the mixture of chlorobromobenzene isomers investigated had m.p. -26° and that when p-chlorobromobenzene was added to it, its melting point changed according to the curve given for a mixture of m- and p-chlorobromobenzenes, it follows that it consisted of 95% of meta- and 5% of para-isomers.

Degradation of Trimethyl Derivative of the Fraction with b. p. 108.5-112° at 11 mm. Similarly, from 2 g of $ClC_6H_4Si(CH_3)_3$, obtained from $ClC_6H_4SiCl_3$ (fraction with b.p. 108.5-112° at 11 mm), and 1.9 g of bromine we obtained 1.3 g (79%) of $(CH_3)_3SiBr$ and 1.5 g (77%) of o-chlorobromobenzene with b.p. 70-72° at 10 mm, d_4^{20} 1.6431, $n^{20}D$ 1.5808. The data obtained showed that the fraction analyzed was o-chlorophenyltrichlorosilane.

d) Degradation of $BrC_6H_4Si(CH_3)_3$ Obtained From Monobromophenyltrichlorosilane, Isolated in the Bromination of $C_6H_5SiCl_3$ in the Presence of Iron. The bromine degradation of monobromophenyltrimethylsilane was carried out similarly. From 17.6 g of silane and 12.5 g of bromine we obtained 9.6 g (83.5%) of $(CH_3)_3SiBr$ and 15.1 g (84.3%) of a colorless liquid, corresponding to dibromobenzene in analysis and having b.p. 89-90° at 11 mm. On standing (18-20°), the liquid partially crystallized. When cooled to 0° it deposited 6.1 g of p-dibromobenzene with m.p. 87° (40.4% of the total weight of the mixture of dibromobenzenes). After separation of the p-dibromobenzene crystals, the liquid residue was cooled to -5° to give 3.8 g (25.1%) of o-dibromobenzene with m.p. 1.5-2.2°, d_{20}^{20} 1.9572. The residue after separation of the o-dibromobenzene crystallized completely at -10°.

According to data in [14], the isomeric p-dibromobenzenes have: para-, m.p. 86.8°, ortho-, m.p. 1.8° $d_4^{20.4}$ 1.9557, meta-, m.p. -6.9°, $d_4^{20.4}$ 1.9523.

SUMMARY

1. A method is described for determining the structure of halogen derivatives of arylchlorosilanes, based on bromine degradation of the products of their exhaustive methylation.

2. By means of this method we determined more accurately the isomeric composition of the monochloro and monobromo derivatives of phenyltrichlorosilane, formed by its halogenation in the presence of iron. In contrast to what we had found previously, it was shown that the chlorination of phenyltrichlorosilane gave mainly (up to 75%) m-chlorophenyltrichlorosilane and in bromination, the main reaction product (up to 70%) was a mixture of p- and o-bromophenyltrichlorosilanes.

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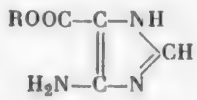
SOME ESTERS OF 4(5)-AMINOIMIDAZOLE-5(4)-CARBOXYLIC ACID

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The only esters of 4(5)-aminoimidazole-5(4)-carboxylic acid described in the literature are the methyl and ethyl esters [1]. The first ester was obtained by catalytic reduction of methyl 4(5)-nitroimidazole-5(4)-carboxylate [2] and the second by condensation of ethyl aminocyanoacetate with formamidine hydrochloride [3]. The hydrochloride and picrate only of the methyl ester are known.

Since derivatives of aminoimidazolecarboxylic acid are of considerable interest from a physiological point of view, we prepared a series of esters of this acid with the general formula



and studied their properties. The starting 4(5)-nitroimidazole-5(4)-carboxylic acid was obtained from 4(5)-hydroxymethylimidazole [4]. The esters of this acid were synthesized by a method described previously [5]. With the exception of the imidazolylmethyl ester of 4(5)-nitroimidazole-5(4)-carboxylic acid, which was reduced with ferrous sulfate in an ammonia medium, all the other nitroesters were reduced with iron filings in the presence of an electrolyte.

The free esters of aminoimidazolecarboxylic acid behaved as bases and gave salts with strong mineral acids and complexes with picric acid with 1 : 1 and 1 : 2 compositions. The hydrochlorides of the esters were white, crystalline substances, which dissolved readily in water, alcohol and ethyl acetate apart from the imidazolylmetlhyl ester, which was more soluble in water than in organic solvents. The free esters were obtained by neutralizing aqueous solutions of the hydrochlorides with sodium carbonate in the cold and subsequent extraction of the base from the dry residue with anhydrous alcohol. The colorless crystals (with the exception of the methyl and isoamyl esters, which were isolated in the form of uncrystallizable oils) were readily soluble in alcohol, acetone and chloroform and considerably less so in water; they gradually darkened and became tarry during storage in air.

The esters were tested pharmacologically (in the form of the hydrochlorides) under the direction of A. S. Saratikov (Tomsk Medical Institute). In contrast to the corresponding esters of nitroimidazolecarboxylic acid, the esters of the amino acid showed hardly any hypotensive action but depressed cardiac activity considerably more strongly than the former; in this respect, the most active was the isoamyl ester (80.7%) and the least active, the ethyl ester of aminoimidazolecarboxylic acid (49.5%).* Only the ethyl ester of benzoylaminoimidazolecarboxylic acid had a clearly expressed antispasmodic action and this ester was also characterized by the lowest toxicity.

EXPERIMENTAL

Methyl 4(5)-Aminoimidazole-5(4)-carboxylate (I). 7.5 g of iron filings, degreased with sodium carbonate, was boiled with 1.5 ml of hydrochloric acid (d 1.19) for 10 minutes. 3 g of methyl 4(5)-nitroimidazole-5(4)-

*Experiments on isolated frog hearts by Straube's method.

Analysis of Esters and Their Hydrochlorides and Picrates

Ester No.	Formula of compounds	% N	
		found	calculated
(II)	$C_6H_9O_2N_3 \cdot C_6H_3O_7N_3$	22.12	21.87
	$C_6H_9O_2N_3 \cdot 2HCl$	18.77	18.42
(III)	$C_7H_{11}O_2N_3 \cdot 2C_6H_3O_7N_3$	20.34	20.09
	$C_7H_{11}O_2N_3 \cdot HCl$	20.79	20.44
	$C_7H_{11}O_2N_3$	24.93	24.85
(IV)	$C_7H_9O_4N_3$	21.02	21.10
(V)	$C_7H_{11}O_2N_3 \cdot C_6H_3O_7N_3$	20.90	21.13
	$C_7H_{11}O_2N_3 \cdot 2HCl$	17.73	17.35
	$C_7H_{11}O_2N_3$	24.28	24.85
(VI)	$C_8H_{13}O_2N_3 \cdot 2C_6H_3O_7N_3$	19.25	19.65
	$C_8H_{13}O_2N_3 \cdot HCl$	18.63	19.13
	$C_8H_{13}O_2N_3$	22.64	22.95
(VII)	$C_8H_{11}O_4N_3$	19.36	19.71
(VIII)	$C_8H_{13}O_2N_3 \cdot 2C_6H_3O_7N_3$	19.50	19.65
	$C_8H_{13}O_2N_3 \cdot HCl$	19.35	19.13
	$C_8H_{13}O_2N_3$	22.59	22.95
(IX)	$C_9H_{15}O_2N_3 \cdot C_6H_3O_7N_3$	19.89	19.72
	$C_9H_{15}O_2N_3 \cdot HCl$	17.67	17.99
(X)	$C_6H_9O_2N_5 \cdot 2C_6H_3O_7N_3$	23.00	23.16
	$C_6H_9O_2N_5 \cdot 2HCl$	24.82	25.00
	$C_6H_9O_2N_5$	33.48	33.82
(XI)	$C_{12}H_{13}O_3N_3$	15.97	16.22

carboxylic acid was introduced with vigorous stirring. The reduction was carried out in a thermostat at 45-47° for 2.5 hours. The reaction mass was filtered, the precipitate washed several times with very weak acid and a saturated solution of picric acid added to the filtrate. The picrate and hydrochloride of the ester were identical with those described in the literature [2].

The ethyl ester (II) was obtained analogously to (I). To improve the solubility of the nitroester, the reduction was carried out in an aqueous alcohol medium. The picrate of the aminoester formed a yellow needles with m.p. 191-192° (from hot water); the hydrochloride formed the hydrochloride, was identical with that described in [3]. Analysis data for the hydrochloride and picrate of this ester and subsequent compounds are given in the table.

The n-propyl ester (III) was obtained analogously to (II). The picrate formed yellow needles with m.p. 167-168°; the hydrochloride gave very fine, colorless crystals (by precipitation with ether from methyl alcohol solution) with m.p. 170-171°. The free ester formed a white powder with m.p. 82-83° (from water).

Isopropyl 4(5)-Nitroimidazole-5(4)-carboxylate (IV). To a solution of 60 ml of isopropyl alcohol and 1.5 ml of sulfuric acid (d 1.84) was added 5 g of 4(5)-nitroimidazole-5(4)-carboxylic acid. The mixture was heated on a boiling water bath for 2 hours. The colorless platelets had m.p. 206-207° (from boiling water). The product was insoluble in cold water, ether, benzene and chloroform and dissolved readily in alcohol, acetone, ethyl acetate and dilute alkalis. It did not give compounds with mineral acids or picric acid.

Isopropyl 4(5)-Aminoimidazole-5(4)-carboxylate (V). This product was obtained analogously to (II). The picrate of the ester formed yellow platelets with m.p. 173-173.5° (from boiling water). The hydrochloride was a white powder with m.p. 97-98° (from a mixture of methanol and ether). The free ester was a white or slightly pinkish powder with m.p. 214-214.5° (from methanol).

n-Butyl 4(5)-Aminoimidazole-5(4)-carboxylate (VI). This product was obtained analogously to (II). The picrate formed yellow needles with m.p. 151-152° (from hot water). The hydrochloride was a white powder with m.p. 128°. The free ester formed colorless needles with m.p. 53-54° (from water).

Isobutyl 4(5)-Nitroimidazole-5(4)-carboxylate (VII). This substance was obtained analogously to (IV) from the nitroacid and primary isobutyl alcohol. The colorless platelets had m.p. 210-211° (from alcohol) and were soluble in hot alcohol.

Isobutyl 4(5)-Aminoimidazole-5(4)-carboxylate (VIII). This product was obtained analogously to (II). The picrate formed fine, yellow crystals with m.p. 170-171° (from hot water). The hydrochloride gave colorless, aggregated crystals with m.p. 175° (with decomp.). The free ester formed colorless needles with m.p. 123-124° (from water).

Isoamyl 4(5)-Aminoimidazole-5(4)-carboxylate (IX). This product was obtained analogously to (II). The picrate gave fine needles with m.p. 152° (from hot water). The hydrochloride was a white powder with m.p. 142-143°, which dissolved in acetone and chloroform.

Imidazolylmethyl 4(5)-Aminoimidazole-5(4)-carboxylate (X). To a solution of 11 g of ferrous sulfate in 10 ml of water was added a hot 10% aqueous solution of imidazolymethyl 4(5)-nitroimidazole-5(4)-carboxylate followed by 12 ml of 25% ammonia solution with stirring; the mixture was heated on a boiling water bath for 5 minutes and filtered hot. The picrate formed yellow needles, which were readily soluble in water and somewhat less so in alcohol. It sublimed readily on heating. The free ester formed fine needles, which were readily soluble in water and hot alcohol and sublimed without melting.

Ethyl 4(5)-Benzoylaminoimidazole-5(4)-carboxylate (XI). 2 g of ethyl 4(5)-aminoimidazole-5(4)-carboxylate in 20 ml of dry xylene was heated on an oil bath and stirred vigorously while 1.4 ml of benzoyl chloride in 10 ml of xylene was added dropwise. The reaction mixture was heated for 5 hours at the boiling point of xylene. The product was collected, dried and recrystallized from dilute alcohol. The colorless crystals had m.p. 190-191°. They were sparingly soluble in water, but dissolved readily in alcohol, acetone and chloroform.

SUMMARY

A series of esters of 4(5)-aminoimidazole-5(4)-carboxylic acid and their hydrochlorides and picrates were prepared. It was established that benzoylation of the amino group lowered the toxicity of the ethyl ester of this acid and conferred an antispasmodic acitvity on it.

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INVESTIGATIONS IN THE FIELD OF BENZIMIDAZOLE DERIVATIVES

II. 1-(2',4'-DINITROPHENYL)-BENZIMIDAZOLE AND 1-METHYL-3-(2',4'-DINITROPHENYL)-BENZIMIDAZOLIUM SALTS*

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N-2,4-Dinitrophenyl derivatives of compounds from the benzimidazole series were unknown until recently. 1-(2',4'-Dinitrophenyl)-2-methylbenzimidazole [2] was described only recently. It seemed interesting to us to study the methods of synthesis and conversions of certain representatives of this class and the benzimidazolium salts formed from them.

We obtained 1-(2',4'-dinitrophenyl)-benzimidazole by fusing benzimidazole with 2,4-dinitrochlorobenzene or by heating these reagents in an alcohol solution in the presence of sodium acetate. In a similar way, a 2,4-dinitrophenyl radical was introduced into the NH group of 2-methylbenzimidazole. Heating 2-amino-2',4'-dinitrodiphenylamine with formic acid did not form a benzimidazole drivative; evidently, cyclization did not occur due to the low basicity of the nitrogen of the NH group and the process stopped at the acylation stage. B. A. Porai-Koshits and Kh. L. Muravich [2] were able to convert 2-amino-2',4'-dinitrodiphenylamine into 1-(2',4'-dinitrophenyl)-2-methylbenzimidazole only by heating the diacetyl derivative of this diamine with 4 N hydrochloric acid at 180°.**

Fusing 1-(2',4'-dinitrophenyl)-benzimidazole with methyl benzenesulfonate formed N-methyl-N'-(2',4'-dinitrophenyl)-benzimidazolium benzenesulfonate. A salt containing the same cation was obtained by the reaction of 1-methylbenzimidazole with 2,4-dinitrochlorobenzene. The identity of the cations of these salts, caused by redistribution of the electron density in the cation after its formation, was demonstrated by conversion of the two salts to the same iodide. Dinitrochlorobenzene also formed a benzimidazolium salt with 5-methoxy-1-methylbenzimidazole but 5-nitro-1-phenylbenzimidazole did not undergo this reaction.

In contrast to the original bases, the benzimidazolium salts obtained reacted readily with aromatic amines, forming 2,4-dinitrophenylarylamines. In this respect they were reminiscent of chloro-2,4-dinitrophenylates of heterocyclic bases, which can also arylate aromatic amines by eliminating the dinitrophenyl radical weakly attached to the onium N-atom [4]. This comparison makes it possible to arrive at the conclusion that the bulk of the cationic charge in N-methyl-N'-dinitrophenylbenzimidazolium salts is borne by the nitrogen atom attached to the dinitrophenyl group and, consequently, to regard chlorides of this type as chloro-2,4-dinitrophenylates of N-methylbenzimidazoles (see, for example, II).

The effect of the dinitrophenyl radical and the onium N-atom produces a strong reduction in the electron density at the C-atom in position 2 in 1-methyl-3-dinitrophenylbenzimidazolium salts.*** This atom therefore

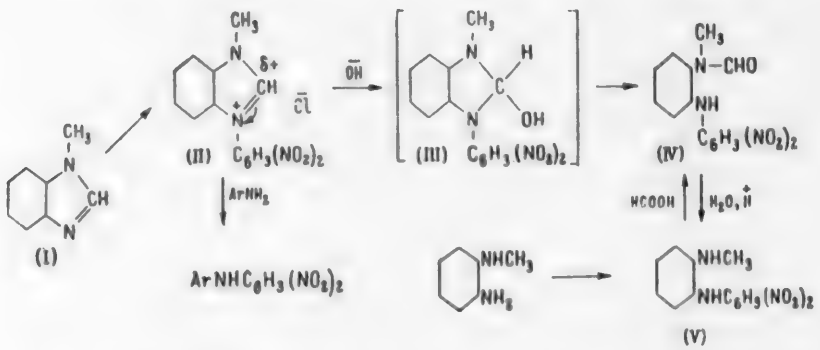
*For communication I see [1].

**On the basis of the data presented, it is hardly possible to accept that the compound obtained by Nietzki and Raillard by heating 2-amino-2',4,4'-trinitro-N-methyldiphenylamine with acetic anhydride and then with dilute sulfuric acid was a benzimidazole derivative, as considered by the authors [3].

***For the distribution of electron density in the imidazole ring of benzimidazole see [5, 1].

readily undergoes attack by a hydroxyl ion, which leads to the formation of so-called pseudobases. The reaction proceeds readily not only under the action of ammonia and sodium carbonate, as was observed, for example, with benzimidazolium salts containing a nitro group [6, 9], but even with such a weak base as pyridine.* The pseudobase** formed from 1-methyl-3-(2',4'-dinitrophenyl)-benzimidazolium salts appeared as yellow crystals with m.p. 174-175°. When treated with dilute hydrochloric acid in the cold or with gentle heating, this compound was not reconverted into the original benzimidazolium salt and in this respect it differed sharply from typical pseudobases of the benzimidazole series [8]. On prolonged heating with 20% hydrochloric acid, the pseudobase formed a solution, which, however, did not contain the original benzimidazolium salt since making it alkaline liberated a precipitate of bright-red crystals with m.p. 177°; in contrast to the pseudobase, this substance dissolved in dilute acids.

In accordance with contemporary ideas on the structure of the products of alkali treatment of benzimidazolium salts [7], these observations led us to assume that the pseudobase of the 1-methyl-3-(2',4'-dinitrophenyl)-benzimidazolium salt precipitated as one of the isomeric acyclic forms. The effect of the dinitrophenyl group caused instability of the cyclic (carbinol) form of the pseudobase (III) and the equilibrium between the tautomeric forms*** was found to be completely displaced toward the formation of the acyclic (amide) form; due to the structural peculiarities of the molecule, the dihydroimidazole ring of form (III) opened in only one direction and led to the formation of only one acyclic form, namely, 2-(N-formylmethylamino)-2',4'-dinitrodiphenylamine (IV). There is no doubt that just this compound was formed and not the isomeric 2-methylamino-2',4'-dinitro-N-formyldiphenylamine since only the former of these has no group with a basic character and therefore could not react with dilute hydrochloric acid, as was observed experimentally. Solution of the pseudobase on prolonged heating with hydrochloric acid was evidently caused by elimination of the formyl from the methylamino group, due to which salt formation became possible.



The accuracy of the hypotheses presented was demonstrated by synthesis of the deformylated pseudobase (V). This compound was found to be identical with the condensation product of 2,4-dinitrochlorobenzene and N-methyl-o-phenylenediamine and thus its structure was undoubtedly that of 2-methylamino-2',4'-dinitrodiphenylamine. As was expected, heating it with formic acid reconverted it into the pseudobase (IV).

Due to the low electron density at the carbon atom in position 2 in N-dinitrophenylbenzimidazole, it seemed that it should have readily undergone nucleophilic substitution. Nonetheless, experiments on the amination of this compound and also 5-nitro-1-phenylbenzimidazole with hydroxylamine did not give positive results as was also observed previously for benzimidazole derivatives of simpler structure [10]. Consequently, in this respect, 1-substituted benzimidazoles differ from derivatives of benzthiazole [11] and quinoline [12], which are readily aminated by hydroxylamine. Due to the high sensitivity of the benzimidazolium salts we synthesized to bases, the action of hydroxylamine on them could not be studied.

*Benzimidazolium salts not containing electrophilic substituents are converted into pseudobases by heating with a concentrated solution of caustic alkali [7].

**We will arbitrarily assign this name to the product formed by the action of alkaline agents on these salts.

***The problem of the tautomerism of pseudobases from the benzimidazole series was examined in one of the previous communications [9].

EXPERIMENTAL

1-(2',4'-Dinitrophenyl)-benzimidazole. 2.45 g of benzimidazole, 4.3 g of 2,4-dinitrochlorobenzene and 2.7 g of crystalline sodium acetate were dissolved in 15 ml of alcohol; the solution was boiled on a water bath for 3 hours under reflux, the volume adjusted to 80 ml with alcohol and the solution heated and filtered hot. The precipitate which formed on cooling was ground with ether, collected by filtration and recrystallized from alcohol. The golden-yellow crystals had m.p. 176° and were readily soluble in chloroform and difficultly so in benzene and ether. The yield was 4.9 g (83%).

The compound was also obtained by fusing 1.7 g of benzimidazole with 2.75 g of 2,4-dinitrochlorobenzene at 90-100° for 2 hours. The melt was cooled and ground with ether. The precipitate was collected and recrystallized from alcohol. The yield was 3.0 g. The presence of potassium fluoride did not promote the reaction (cf. [13]).

Found %: C 55.21, 54.81; H 3.28, 3.02; N 19.83, 19.81. $C_{13}H_8O_4N_4$. Calculated %: C 54.94; H 2.84; N 19.71.

2-Formylamino-2',4'-dinitrodiphenylamine. A solution of 1.0 g of 2-amino-2',4'-dinitrodiphenylamine in 10 ml of 85% formic acid with the addition of 2 drops of hydrochloric acid was boiled for 3 hours under reflux. The cooled mixture was diluted with water and neutralized with ammonia. The yield was 1.0 g (90%). The yellowish white crystals (from alcohol) with m.p. 183° were soluble in hot benzene and insoluble in dilute hydrochloric acid.

Found %: N 18.47, 18.62. $C_{13}H_{10}O_5N_4$. Calculated %: N 18.54.

1-Methyl-3-(2',4'-dinitrophenyl)-benzimidazolium Benzenesulfonate. A mixture of 0.20 g of 1-(2',4'-dinitrophenyl)-benzimidazole with 0.15 g of methyl benzenesulfonate was heated to 135° and heated at this temperature for a further 15 minutes. The cooled melt was ground with benzene and the precipitate collected. The yield was 0.30 g. The greenish yellow crystals (from alcohol) had m.p. 208° and were readily soluble in water.

Found %: C 52.84, 52.66; H 3.83, 3.69; S 7.08, 6.89. $C_{20}H_{16}O_7N_4S$. Calculated %: C 52.63; H 3.53; S 7.03.

1-Methyl-3-(2',4'-dinitrophenyl)-benzimidazolium Iodide. The compound was obtained by adding a 50% solution of potassium iodide to a saturated aqueous solution of 1-methyl-3-(2',4'-dinitrophenyl)-benzimidazolium benzene sulfonate or chloride. The bright orange crystals (from alcohol) had m.p. 197°.

Found %: I 29.91, 29.93. $C_{14}H_{11}O_4N_4I$. Calculated %: I 29.78.

1-Methyl-3-(2',4'-dinitrophenyl)-benzimidazolium Chloride (II). A mixture of 1.0 g of 1-methylbenzimidazole and 2.0 g of 2,4-dinitrochlorobenzene was heated on a boiling water bath for 2-3 hours with periodic stirring. The cooled melt was ground with ether and filtered. The precipitate was recrystallized from alcohol. The yield was 2.0 g (79%). The white crystals with m.p. 232-233° were readily soluble in water. The chloride was not formed in acetone (cf. [16]).

Found %: Cl 10.53, 10.57. $C_{14}H_{11}O_4N_4Cl$. Calculated %: Cl 10.59.

Interaction of 1-Methyl-3-(2',4'-dinitrophenyl)-benzimidazolium Salts With Aromatic Amines. A mixture of 0.70 g of 1-methyl-3-(2',4'-dinitrophenyl)-benzimidazolium benzenesulfonate and 0.60 g of aniline was heated to 100° on a water bath over a period of 0.5 hours and then heated on a boiling water bath for a further 2-3 hours. The cooled mixture was treated with 7 ml of 10% hydrochloric acid and the precipitate collected and washed with water. The product obtained melted at 157°; a mixed melting point with authentic 2,4-dinitrodiphenylamine was not depressed. The yield was 0.35 g (87%).

The interaction of 0.20 g of 1-methyl-3-(2',4'-dinitrophenyl)-benzimidazolium chloride with 0.15 g of p-anisidine under the same conditions yielded 0.14 g (82%) of a substance with m.p. 141°, which was 4-methoxy-2',4'-dinitrodiphenylamine.

2-(N-Formylmethylamino)-2',4'-dinitrodiphenylamine [pseudobase of 1-methyl-3-(2',4'-dinitrophenyl)-benzimidazolium salts] (IV). To a solution of 0.5 g of 1-methyl-3-(2',4'-dinitrophenyl)-benzimidazolium

chloride in 15 ml of water was gradually added 1 ml of 25% ammonia. When rubbed with a rod, the viscous orange precipitate initially formed changed to yellow crystals, which were collected, washed with water and recrystallized from alcohol. The yield was almost quantitative. The light-yellow crystals with m.p. 174-175° were readily soluble in chloroform. The pseudobase was also formed in quantitative yield by the action of sodium carbonate and pyridine in the cold or excess sodium acetate on heating.

The compound was also obtained by heating a mixture of 0.80 g of 1-methylbenzimidazole and 1.2 g of 2,4-dinitrochlorobenzene with 2 ml of alcohol on a water bath for 2 hours. The yield was 0.90 g (47%). The formation of a pseudobase under these conditions is evidently explained by decomposition of the quaternary salt formed in the first stage of the reaction under the action of a base, namely, the unreacted 1-methylbenzimidazole. Actually, heating an alcohol solution of 1-methyl-3-(2',4'-dinitrophenyl)-benzimidazolium chloride with 1-methylbenzimidazole formed the pseudobase. The salt was not decomposed in the absence of 1-methylbenzimidazole.

Found %: C 52.95, 53.22; H 4.04, 3.84; N 17.82, 17.70. $C_{14}H_{12}O_6N_4$. Calculated %: C 53.17; H 3.82; N 17.72.

2-Methylamino-2',4'-dinitrodiphenylamine (V). a) A solution of 0.50 g of N-methyl-o-phenylenediamine dihydrochloride 0.60 g of 2,4-dinitrochlorobenzene and 2.1 g of sodium acetate in 15 ml of alcohol was boiled for 2 hours; the precipitate formed was collected and recrystallized from alcohol. The yield was 0.60 g (80%). The bright-red crystals with m.p. 177° were soluble in dilute hydrochloric acid. When heated to boiling over a period of 0.5 hours with formic acid, the compound was converted to 2-(N-formylmethylamino)-2',4'-dinitrodiphenylamine [pseudobase (IV)].

The starting N-methyl-o-phenylenediamine dihydrochloride [14] was obtained by reduction of N-methyl-o-nitroaniline, synthesized from N-benzenesulfonyl-o-nitroaniline [15].

b) A suspension of 0.30 g of pseudobase with structure (IV) in 15 ml of hydrochloric acid (1 : 2) was boiled for 1-2 hours until the precipitate dissolved. The cooled solution was neutralized with ammonia. The precipitate was collected, washed with water and recrystallized from alcohol. The yield was 0.22 g (81%). The bright-red crystals had m.p. 177°. A mixed melting point of this product and 2-methylamino-2',4'-dinitrodiphenylamine, obtained according to "a", was not depressed.

Found %: C 54.01, 54.20; H 4.25, 4.24; N 19.59, 19.50. $C_{13}H_{12}O_4N_4$. Calculated %: C 54.16; H 4.20; N 19.44.

1,2-Dimethyl-3-(2',4'-dinitrophenyl)-benzimidazolium Benzenesulfonate. This compound was obtained in almost quantitative yield by fusing 2.0 g of 1-(2',4'-dinitrophenyl)-2-methylbenzimidazole with 2.72 g of methyl benzenesulfonate at 90° for 15-20 minutes. The greenish yellow crystals (from alcohol) with m.p. 227-228° were soluble in water. The introduction of ammonia to an aqueous solution of the salt precipitated a pseudobase; treatment of this with boiling hydrochloric acid (1 : 2) and then ammonia yielded a substance with m.p. 177°, which was identical with the deformylation product from the pseudobase (IV).

Found %: S 6.69, 6.85. $C_{21}H_{18}O_7N_4S$. Calculated %: S 6.82.

We prepared the starting 1-(2',4'-dinitrophenyl)-2-methylbenzimidazole, which was described previously [2], by fusing equimolecular amounts of 2-methylbenzimidazole and 2,4-dinitrochlorobenzene at 120° for 3 hours or by heating these reagents in an alcohol solution in the presence of sodium acetate. In contrast to benzimidazole itself, under these conditions its 2-methyl derivative did not form the free base but the hydrochloride (m.p. 210°). For preparing the base, a solution of the salt in alcohol was treated with ammonia.

1-Methyl-3-(2',4'-dinitrophenyl)-5-methoxybenzimidazolium Chloride. To prevent tar formation, 1-methyl-5-methoxybenzimidazole had to be heated with dinitrochlorobenzene at a lower temperature than in the case of 1-methylbenzimidazole, but for a longer time. The experiment was carried out at 60° for 5 hours. The melt was dissolved in the minimal amount of alcohol and the solution diluted with five times the volume of ether. The precipitate was collected and washed with ether. The yield was 44%. The colorless crystals (from a mixture of alcohol and ether) with m.p. 210° were readily soluble in water. Addition of ammonia to an aqueous solution of the salt liberated a viscous, orange precipitate of the pseudobase, which rapidly became yellow.

Found %: Cl 9.59, 9.65. $C_{15}H_{13}O_6N_4Cl$. Calculated %: Cl 9.72.

SUMMARY

1. When treated with 2,4-dinitrochlorobenzene, benzimidazole and its 2-methyl derivative readily formed N-dinitrophenyl derivatives.

2. 1-Methylbenzimidazoles reacted with 2,4-dinitrochlorobenzene to form 1-methyl-3-(2',4'-dinitrophenyl)-benzimidazolium salts. Salts with the same cation could also be obtained starting from N-dinitrophenylbenzimidazole and its derivatives.

3. 1-Methyl-3-(2',4'-dinitrophenyl)-benzimidazolium salts reacted with aromatic amines with the elimination of the dinitrophenyl radical and the formation of diphenylamine derivatives.

4. The action of alkaline agents on 1-methyl-3-(2',4'-dinitrophenyl)-benzimidazolium salts produced opening of the imidazole ring and the formation of one of the isomeric amide (acyclic) forms of the pseudobase, namely, 2-(N-formylmethylamino)-2',4'-dinitrodiphenylamine. The structure of the deformylation product of the pseudobase was demonstrated by synthesis.

5. New evidence was obtained of the existence of so-called pseudobases of benzimidazolium salts in acyclic forms.

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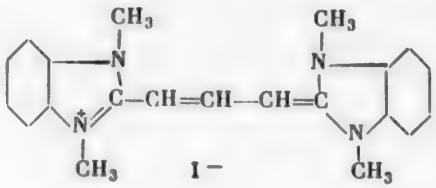
CYANINE DYES CONTAINING FLUORINE

VII. SYNTHESIS OF CYANINE DYES FROM 6-TRIFLUOROMETHYL- AND 6-TRIFLUOROMETHYLSULFONYLBENZIMIDAZOLE

L. M. Yagupol'skii and V. I. Troitskaya

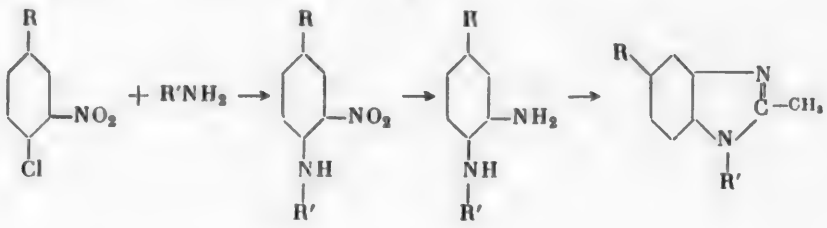
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Cyanine dyes that are derivatives of benzimidazole have received little attention. The simplest dye of this series, 1,1',3,3'-tetramethylimidocarbocyanine iodide, was prepared by Ogata [1] and then A. I. Kiprianov [2],

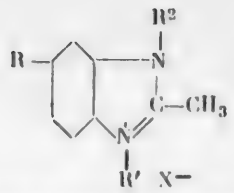


who investigated its absorption spectrum in the visible and ultraviolet parts of the spectrum. A series of patents on the preparation of symmetrical and unsymmetrical imidocarbocyanines and their application to the sensitization of photographic emulsions was taken out by the firm I. G. Farben Industrie [3]. These dyes contained methyl or alkoxyl groups and also a chlorine atom in the hetero residues. This firm took out a separate patent on unsymmetrical dyes containing a trifluoromethyl group in the benzimidazole residue [4]. Patents were recently taken out on the use of 5,5'-dichloro-, 5,5',6,6'-tetrachloro-, 5,5'-dibromo- and 5,5'-diacetylimidocarbocyanines in a mixture with other dyes [5].

The purpose of the present work was to synthesize imidocarbocyanines containing the electron-acceptor trifluoromethyl and trifluoromethylsulfonyl groups as substituents. The benzimidazole derivatives required for this were synthesized according to the scheme



The bases obtained were converted into quaternary salts:



R = CF_3, CF_3SO_2;
R′ = C_2H_5, C_6H_5, α-$C_{10}H_7$;
R^2 = CH_3, C_2H_5.

These quaternary salts were used to synthesize the cyanine dyes whose formulas and absorption maxima in ethyl alcohol are presented in Tables 1 and 2. The absorption maxima of dyes not containing trifluoromethyl groups are given in brackets. The absorption curves were plotted on an SF-4 spectrophotometer. The symmetrical imidocarbocyanines were obtained by boiling the quaternary salts with orthoformic ester in nitrobenzene by Van Dormael's method [6].

The introduction of trifluoromethyl [7] and trifluoromethylsulfonyl groups [8] into the benzthiazole ring of thiacarbocyanine hardly changed the absorption maximum of the dye. With imidocarbocyanine containing a trifluoromethyl group in position 6 (I), the absorption maximum was displaced towards longer wavelengths by 9 mμ and by 24 mμ when a trifluoromethylsulfonyl group was introduced (V). Table 2 gives the formulas and absorption maxima of two unsymmetrical cyanine dyes and two rhodocyanines. The unsymmetrical imidocarbocyanine with a CF_3 group (X) obeyed A. I. Kiprianov's rule [9] on the hypsochromic shift of the absorption maximum (a deviation of the arithmetic mean of the two mother dyes by 11 mμ towards shorter wavelengths). It is interesting that replacement of the methyl by ethyl radicals at the N atoms of the benzimidazole nucleus produced a considerable change in the absorption maximum of imidocarbocyanines. Thus, for example, replacement of two methyl by ethyl radicals [dyes (III) and (IV), and (VI) and (VII)] produced a shift in the absorption maximum towards longer wavelengths by 7-8 mμ and replacement of four methyls by ethyl radicals [dyes (I) and (II)], a shift of 13 mμ. Replacement of a phenyl radical by a naphthyl did not affect the absorption maximum [dyes (VII) and (VIII)].

Data on the photographic properties of the cyanine dyes containing fluorine will be reported later.

EXPERIMENTAL

3-Nitro-4-chlorobenzotrifluoride was prepared from p-chlorotoluene [10]. The latter was chlorinated in the side chain, the chlorine replaced by fluorine with antimony trifluoride and the product obtained was nitrated [11].

2-Nitro-4-trifluoromethyldiphenylamine. 31 g of 3-nitro-4-chlorobenzotrifluoride and 62 g of aniline were heated on an oil bath for 3.5 hours at 140-150°. The precipitate that formed on cooling was transferred to a 10% solution of hydrochloric acid, the precipitate collected by filtration and washed with 10% hydrochloric acid and water. The yield, after the product had been recrystallized from methyl alcohol, was 37 g (95.3%) and the m.p. 84-85°.

Found %: N 9.68, 9.80. $C_{13}H_9O_2N_2F_3$. Calculated %: N 9.93.

2-Amino-4-trifluoromethyldiphenylamine. 37 g of 2-nitro-4-trifluoromethyldiphenylamine was dissolved in 150 ml of methyl alcohol and heated with a solution of 118.4 g of stannous chloride in 93 ml of concentrated hydrochloric acid for 3 hours on a boiling water bath. When the product had been recrystallized from aqueous methyl alcohol, the yield was 29.6 g (90.0%) and the m.p. 102-104°.

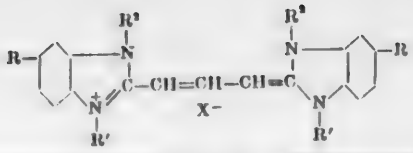
Found %: N 11.04, 10.82. $C_{13}H_{11}N_2F_3$. Calculated %: N 11.11.

2-Methyl-3-phenyl-6-trifluoromethylbenzimidazole. A solution of 6 g of 2-amino-4-trifluoromethyldiphenylamine in 20 ml of benzene was mixed with a solution of 3.6 g of acetyl chloride in 5 ml of benzene and boiled for 2 hours. The benzene was removed in distillation and the product dissolved in water, acidified with hydrochloric acid. The base was precipitated with ammonia. The yield was 5.9 g (89.5%) and the m.p. 117-118° (from aqueous methyl alcohol).

Found %: N 10.00, 10.09. $C_{15}H_{11}N_2F_3$. Calculated %: N 10.11.

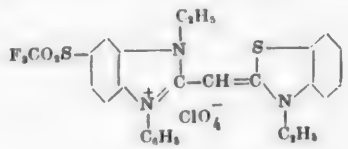
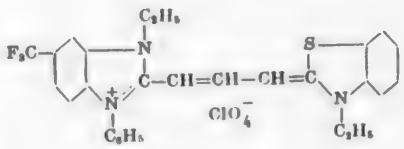
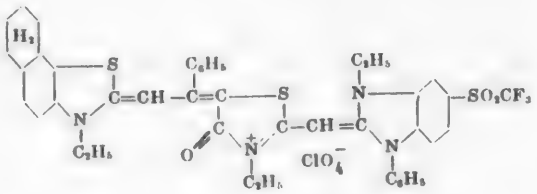
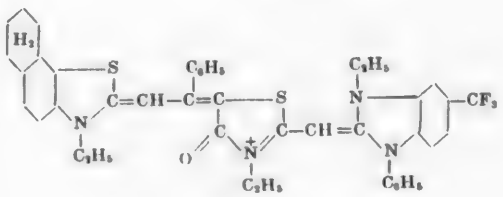
3-Nitro-4-aminobenzotrifluoride was obtained from 3-nitro-4-chlorobenzotrifluoride [11].

TABLE 1



No.	R	R'	R^2	X	λ_{max} (in mμ)
(I)	CF_3	CH_3	CH_3	I^-	494 (491)
(II)	CF_3	C_2H_5	C_2H_5	I^-	507 (498)
(III)	CF_3	C_6H_5	CH_3	ClO_4^-	504
(IV)	CF_3	C_6H_5	C_2H_5	I^-	511
(V)	SO_2CF_3	C_2H_5	C_2H_5	I^-	522
(VI)	SO_2CF_3	C_6H_5	CH_3	I^-	518
(VII)	SO_2CF_3	C_6H_5	C_2H_5	ClO_4^-	525
(VIII)	SO_2CF_3	α-$C_{10}H_7$	C_2H_5	ClO_4^-	525

TABLE 2

No.	Formula	λ_{max} (in mμ)
(IX)		426
(X)		521
(XI)		616
(XII)		600

3,4,-Diaminobenzotrifluoride was obtained by reduction of 3-nitro-4-aminobenzotrifluoride [12].

2-Methyl-6-trifluoromethylbenzimidazole. 7.74 g of 3,4-diaminobenzotrifluoride, 12 ml of acetic anhydride and 39 ml of 15% hydrochloric acid were mixed and boiled for 2 hours. The base was precipitated with ammonia. When the product had been recrystallized from aqueous alcohol, the yield was 7.6 g (86.4%) and the m.p. 187-188°.

Found %: N 14.06, 14.27. $C_9H_7N_2F_3$. Calculated %: N 14.00.

3-Nitro-4-ethylaminophenyl Trifluoromethyl Sulfone. 1 g of 3-nitro-4-chlorophenyl trifluoromethyl sulfone (m.p. 55-56° [8]) was heated with 2.2 ml of a 20% alcohol solution of ethylamine in a sealed tube for 2.5 hours at 90-100° and for 5 hours at 110°. The precipitate was collected and washed with water. After recrystallization of the product from alcohol, the yield was 0.85 g (82.5%) and the m.p. 105-107°.

Found %: N 8.85, 8.99. $C_9H_9O_4N_2SF_3$. Calculated %: N 9.39.

3-Amino-4-ethylaminophenyl Trifluoromethyl Sulfone. A solution of 2.84 g of 3-nitro-4-ethylaminophenyl trifluoromethyl sulfone in 20 ml of alcohol was mixed with a solution of 7.5 g of stannous chloride in 16 ml of concentrated hydrochloric acid and boiled for 1 hour. After recrystallization of the product from benzene, the yield was 2.18 g (85.0%) and the m.p. 146-147°.

Found %: N 10.20, 10.13. $C_9H_{11}O_2N_2SF_3$. Calculated %: N 10.45.

2-Methyl-3-ethyl-6-trifluoromethylsulfonylbenzimidazole. A solution of 2.1 g of 3-amino-4-ethylaminophenyl trifluoromethyl sulfone in 3 ml of benzene was mixed with a solution of 1.23 g of acetyl chloride in 2 ml of benzene and boiled for 3 hours. The benzene was removed by distillation, the solid residue dissolved in 20% hydrochloric acid and the base precipitated with ammonia. After recrystallization of the product from aqueous methyl alcohol, the yield was 2.13 g (93.0%) and the m.p. 163-164°.

Found %: N 9.63, 9.69. $C_{11}H_{11}O_2N_2SF_3$. Calculated %: N 9.60.

2-Methyl-3-phenyl-6-trifluoromethylsulfonylbenzimidazole had m.p. 190-191° [8].

2-Nitro-4-trifluoromethylsulfonylphenyl-α-naphthylamine. 5 g of 3-nitro-4-chlorophenyl trifluoromethyl sulfone and 10 g of α-naphthylamine were heated on an oil bath for 6 hours at 130-140° and at the end the temperature was raised to 170°. The α-naphthylamine was washed out by boiling with a large amount of 10% hydrochloric acid and washing with water and a small amount of hot methyl alcohol. When the product had been recrystallized from methyl alcohol, the yield was 6.13 g (90.0%) and the m.p. 130-131°.

Found %: N 7.38, 7.36. $C_{17}H_{11}O_4N_2SF_3$. Calculated %: N 7.07.

2-Amino-4-trifluoromethylsulfonylphenyl-α-naphthylamine. A suspension of 5.12 g of 2-nitro-4-trifluoromethylsulfonylphenyl-α-naphthylamine in 20 ml of alcohol was mixed with a solution of 10.2 g of stannous chloride in 7.3 ml of hydrochloric acid and boiled for 2 hours on a water bath. After recrystallization of the product from aqueous methanol, the yield was 4.3 g (92.0%) and the m.p. 170-171°.

Found %: N 8.09, 7.91. $C_{17}H_{13}O_2N_2SF_3$. Calculated %: N 7.65.

2-Methyl-3-naphthyl-6-trifluoromethylsulfonylbenzimidazole. A mixture of 0.9 g of 2-amino-4-trifluoromethylsulfonylphenyl-α-naphthylamine and 30 ml of acetic anhydride was boiled for 4.5 hours, 30 ml of 4 N hydrochloric acid added and the mixture boiled for a further 2 hours. The acetic and hydrochloric acids were removed in a water pump vacuum. The product was dissolved by boiling with 30 ml of 4 N hydrochloric acid and the base precipitated with ammonia. After recrystallization of the product from aqueous methyl alcohol, the yield was 0.6 g (62.5%) and the m.p. 150-152°.

Found %: N 7.35, 7.46. $C_{19}H_{13}O_2N_2SF_3$. Calculated %: N 7.18.

Methylmethosulfate of 2,3-dimethyl-6-trifluoromethylbenzimidazole (A) was obtained by heating 1 mole of base with 3 moles of dimethyl sulfate for 4 hours at 110-120°. The product was washed with ether and the iodide precipitated by the addition of a saturated solution of potassium iodide.

The ethyltosylate of 2-methyl-3-ethyl-6-trifluoromethylbenzimidazole (B) was obtained by heating 1 mole of base with 3 moles of ethyl p-toluenesulfonate for 5 hours at 140-150°. The product was washed with ether and the iodide precipitated by the addition of a saturated solution of potassium iodide.

TABLE 3

Dyes (see Table 1)	Quatenary salts	Anion	Boiling time (in hours)	Recrystallization solvent	Yield (in %)	Melting point (with decomp.)	External form of dye	Empirical formula	Analysis data		
									element	found (in %)	calculated (in %)
(I)	A	I^-	6	CH_3OH	7.3	255—258°	Orange-red needles	$C_{23}H_{21}N_4IF_6$	I	21.12, 21.29	21.38
(II)	B	I^-	1	CH_3OH	11.7	251—252	Orange-red needles	$C_{27}H_{29}N_4IF_6$	I	19.34, 19.65	19.53
(III)	C	ClO_4^-	2	$CH_3OH + H_2O$	10.3	250—253	Dark red needles	$C_{33}H_{25}N_4O_4ClF_6$	N	8.08, 8.12	8.11
(IV)	H	I^-	2	$CH_3OH + H_2O$	46.5	232—235	Light red needles	$C_{35}H_{29}N_4IF_6$	I	17.24, 17.10	17.16
(V)	F	I^-	2	CH_3OH	20.0	255—257	Red needles	$C_{27}H_{29}N_4O_4S_2IF_6$	I	16.36, 16.43	16.32
(VI)	O	I^-	2	$CH_3OH + H_2O$	21.0	232—233	Dark red needles	$C_{33}H_{25}O_4N_4S_2IF_6$	I	14.90, 15.06	15.01
(VII)	E	ClO_4^-	3	$CH_3OH + H_2O$	30.0	230—232	Light red needles	$C_{35}H_{29}S_2O_8N_4ClF_6$	N	6.64, 6.73	6.62
(VIII)	G	ClO_4^-	1 hour at 185-190° (in bath)	$C_2H_5OH + H_2O$	21.3	284—286	Dark red prisms	$C_{43}H_{33}O_8N_4S_2ClF_6$	N	5.91, 5.98	5.92

The methylmethosulfates of 2-methyl-3-phenyl-6-trifluoromethyl- (C) and 2-methyl-3-phenyl-6-trifluoromethylsulfonylbenzimidazole (D) were obtained by heating 1 mole of base with 1.2 moles of dimethyl sulfate for 5 hours at 110-120°. The cooled product was washed with ether, dissolved in water and the iodide or perchlorate precipitated by the addition of a saturated solution of potassium iodide or sodium perchlorate.

The ethyltosylates of 2-methyl-3-phenyl- (E), 2-methyl-3-ethyl- (F), 2-methyl-3-naphthyl-6-trifluoromethylsulfonylbenzimidazole (G) and 2-methyl-3-phenyl-6-trifluoromethylbenzimidazole (H) were obtained by heating 1 mole of base with 1.2 moles of ethyl p-toluenesulfonate for 4-5 hours at 140-150°. On cooling, the quaternary salts solidified and were washed with ether. The iodides or perchlorates were precipitated from aqueous solutions of the ethyltosylates of the quaternary salts with a saturated aqueous solution of potassium iodide or sodium perchlorate.

Dyes. All the symmetrical dyes (see Table 1) were prepared by boiling 2 g of quaternary salt with 2 ml of orthoformic ester and 10 ml of nitrobenzene; they were precipated and washed with ether. Table 3 gives the preparation conditions, yields and melting points of the symmetrical imidocarbocyanines.

The unsymmetrical dyes and rhodocyanines were obtained in the following way.

1-Ethyl-3-phenyl-6-trifluoromethylsulfonylbenzimidazole-(2)-3'-ethylbenzthiazole-(2')-monomethynecyanine Perchlorate (IX). 0.47 g of the ethylperchlorate of 2-methyl-3-phenyl-6-trifluoromethylsulfonylbenzimidazole, 0.34 g of the iodoethylate of 2-methylmercaptobenzthiazole, 0.1 g of triethylamine and 5 ml of anhydrous alcohol were boiled for 1 hour and left overnight and then the dye collected, washed with water and recrystallized from alcohol. The product formed yellow needles. The yield was 0.16 g (25.4%) and the m.p. 189-191° (with decomp.).

Found %: N 6.60, 6.55. $C_{26}H_{23}O_6N_3S_2ClF_3$. Calculated %: N 6.67.

1-Ethyl-3-phenyl-6-trifluoromethylbenzimidazole-(2)-3'-ethylbenzthiazole-(2')-trimethynecyanine Perchlorate (X). 0.43 g of 2-methyl-3-phenyl-6-trifluoromethylbenzimidazole iodoethylate, 0.45 g of 2-ω-acetanilidovinylbenzthiazole iodoethylate, 5 ml of anhydrous alcohol and 0.1 g of triethylamine were boiled together for 2 hours. The dye obtained was converted into the perchlorate. On recrystallization from alcohol, it formed dark red prisms. The yield was 0.09 g (15.3%) and the m.p. 254-256° (with decomp.).

Found %: N 7.23, 7.25. $C_{28}H_{25}O_4N_3SClF_3$. Calculated %: N 7.10.

1'-Ethyl-3'-phenyl-6'-trifluoromethylsulfonylbenzimidazole-(2')-3-ethyl-4-keto-5-[(3"-ethyl-6",7"-tetramethylenebenzthiazolinylidene-2")-α-phenylethylidene]-thiazole-(2)-methynecyanine Perchlorate (XI). 0.48 g of 3-ethyl-4-keto-5-[(3'-ethyl-6',7'-tetramethylenebenzthiazolinylidene-2')-α-phenylethylidene]-merocyanine and 0.38 g of dimethyl sulfate were heated at 120-125° for 30 minutes. The crimson melt obtained solidified to a crystalline mass, which was washed with absolute ether. To the reaction mass was added 0.5 g of 2-methyl-3-phenyl-6-trifluoromethylsulfonylbenzimidazole ethylperchlorate and 4 ml of pyridine and the mixture heated for 3 hours with a bath temperature of 125°. The product was recrystallized from alcohol. It formed black needles. The yield was 0.07 g (7.65%) and the m.p. 244-246° (with decomp.).

Found %: N 5.6, 5.72. $C_{43}H_{40}O_7N_4S_3F_3Cl$. Calculated %: N 6.13.

1'-Ethyl-3'-phenyl-6'-trifluoromethylbenzimidazole-(2')-3-ethyl-4-keto-5-[(3"-ethyl-6",7"-tetramethylenebenzthiazolinylidene-2")-α-phenylethylidene]-thiazole-(2)-methynecyanine Perchlorate (XII). This substance was obtained analogously to the previous dye from 0.4 g of the same merocyanine 0.38 g of dimethyl sulfate and 0.5 g of 3-phenyl-6-trifluoromethylbenzimidazole ethylperchlorate. The product was recrystallized from alcohol. It formed black needles. The yield was 0.08 g (9.5%) and the m.p. 299-301° (with decomp.).

Found %: S 7.54 7.62. $C_{43}H_{40}O_5N_4S_2ClF_3$. Calculated %: S 7.54.

SUMMARY

The synthesis of 2-methyl-3-phenyl-6-trifluoromethyl- and 2-methyl-3-ethyl-6-trifluoromethylsulfonylbenzimidazoles is described. These bases and also 2-methyl-3-phenyl-6-trifluoromethylsulfonylbenzimidazole which we described previously were converted into quaternary salts from which we obtained 8 symmetrical imidocarbocyanines, 2 unsymmetrical ones and 2 rhodocyanines. It was shown that the introduction of a trifluoro-

methyl group into position 6 of the benzimidazole nucleus produced a shift in the absorption maximum toward longer wavelengths by 9 mμ and a trifluoromethylsulfonyl group by 24 mμ in comparison with unsubstituted 1 1',3,3'-tetraethylimidocarbocyanine.

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STUDY OF THE REACTION OF CHROMATE WITH DIPHENYLCARBAZIDE

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The formation of an intensely colored compound by the interaction of chromates with diphenylcarbazide (subsequently referred to as DC) has been used widely in chemical analysis. Nonetheless, the problem of the chemistry of this reaction still produces lively discussion. There are two main points of view: 1) the action of chromate oxidizes DC to diphenylcarbazone (DCO) and at the moment of its formation, the tri- or divalent chromium produced gives a colored complex with DCO; 2) by a reaction proceeding through intermediate stages, DC is oxidized to form a certain colored product so that the color of the final product is not caused by complex formation. From this point of view, the colored product from the reaction of chromate with DC differs from the colored compounds formed by the reaction of DC or DCO with many ions (mercury, molybdate, copper etc.). A series of new papers has recently appeared on this problem. Without going into many details on the work, in Table 1 we give the basic data on the methods and results of different investigators.

As Table 1 shows, there are contradictory data. Some arguments (3b, 4 and 5a) are not sufficiently convincing and the experimental data may be explained by other and even opposite points of view. Certain data are simply incorrect and are explained by the insufficient purity of the DC and DCO or by other reasons in general (see below). Thus, contrary to the data in [4, 5], pure DCO did not react with chromate [6] as was also confirmed by our data. For this purpose we purified DC by the method in [7] and DCO by the method in [8]. The preparation obtained had m.p. 172° (DC) and 127° (DCO), which agree with literature data.

A study of the data [5] on the reaction of trivalent chromium with DCO in the presence of an acetate buffer showed us the following. In the presence of acetic acid, but with chromium compounds completely absent from the solution, DCO formed a colored compound, which was soluble in chloroform and benzene but insoluble in isoamyl alcohol. Under these conditions DCO formed such a compound immediately, while DC did so after standing in air. It is interesting that the formation of this compound did not depend on the pH as chloroform extractedan intensely colored compound from a solution of 10 N sulfuric acid.

Our data on purified DCO showed that in the absence of acetic acid it did not react with hexavalent, trivalent or divalent chromium. It was further established that when DC was mixed with a solution of divalent chromium in sulfuric acid solution, it did not form a colored compound, contrary to data given in the literature that divalent chromium reacted with DCO [4-7]. The data given in the literature show that in all cases the acetate of divalent chromium was used; apparently, the colored compound was formed as a result of DCO reacting with acetic acid and not with Cr^{2+}. The color intensity of the solution of the substance formed by the reaction of divalent chromium with DC in sulfuric acid solution was considerably less (by a factor of ~125) than that of the substance formed by the reaction of an equivalent amount of hexavalent chromium under similar conditions.

In spite of new data in the literature, there is essentially no direct proof as to whether the colored compound formed by the reaction of chromates with DC is a chromium complex similar to the complexes of DCO with mercury, copper etc.,or whether it is simply a particular product of DC oxidation. To us, the following seemed the most satisfactory way of solving the problem.

a) A Study of the Extraction of the Colored Compound. Isoamyl alcohol was used for extracting the colored product formed by reacting Cr^{VI} with DC. Cyclohexanone and some other solvents could also be used. The

TABLE 1

Expt. No.	Author's conclusion on the character of the colored compound	Method and means of proof
1	Cr^{3+} – DCO complex [1, 2]	After a time weakly acid solutions gave an amorphous violet precipitate of variable composition containing chromium.
2	DC oxidation product; chromium was not part of the composition of the colored complex [3]	a) Formation of the reaction product was promoted by an increase in the acidity of the medium, which increased the oxidation potential of chromate; on the contrary, the formation of complexes of metals with DC was promoted by an increase in pH. b) The colored compound was appreciably (distribution coefficient ~0.5) extracted with amyl alcohol in strongly acid medium; chromium remained mainly in the aqueous phase.
3	Cr^{3+} – DCO complex [4]	a) The reactions Cr^{VI} + DC, Cr^{VI} + DCO, Cr^{II} + DCO gave substances with the same absorption spectra. b) The maximum optical density for the Cr^{II} + DCO reaction was found at a 1:1 ratio and for the Cr^{IV} + DC reaction, at a 2:3 ratio, which was explained by the consumption of 1 mole of DC for the reduction $Cr^{VI} \rightarrow Cr^{II}$.
4	Cr^{3+} – DCO complex [5]	A violet color was observed in the DCO + Cr^{III} reaction in an aqueous alcohol solution in the presence of acetate; the colored compound was extracted with chloroform and benzene.
5	Cr^{3+} – DCO complex [6]	a) A solution of the Cr^{III} salt in dimethylformamide gave with DCO a red-violet color (λ_{max} 550 mμ). b) The colored compound formed in the Cr^{VI} – DC reaction was extracted with isoamyl alcohol; chromium was detected in the extract.

colored compound was not extracted fully from sulfuric acid solution with isoamyl alcohol. However, if a large excess of sodium chloride was added to the solution, the whole of the colored compound passed into the alcohol extract. In order to establish whether there was chromium in the composition of the colored compound extracted with isoamyl alcohol or whether it remained in the aqueous solution, the alcohol extract and the aqueous solution were evaporated to dryness and the residues treated with perchloric acid. After decomposition of the organic substances, the solutions were made alkaline with sodium peroxide to oxidize the chromium. The chromium was determined by reaction with DC. Four series of experiments were carried out. The only difference in them was the conditions of extracting the colored compound (see Table 2). Control experiments showed that in the absence of DC, chromium that had been reduced from an appropriate amount of potassium dichromate (with ferrous sulfate) could not be extracted under the given conditions. In all cases, 10 ml of a 0.1% solution of DC in 0.2 N or 1.5 N sulfuric acid was used and 10 ml of a 0.001 N solution of potassium dichromate (representing 0.15 mg of chromium) was added slowly. In all cases, one extraction with 20 ml of isoamyl alcohol was made. The experimental results are given in Table 2.

TABLE 2

Effect of Medium on the Extent of Extraction of the Colored Compound

Expt. No.	Medium	Extent of extraction of colored compound	Extent of chromium extraction
1	0.2 N H_2SO_4	10%	10%
2	0.2 N H_2SO_4, saturated with sodium chloride	Complete	Complete
3	1.5 N H_2SO_4	50%	20%
4	1.5 N H_2SO_4, saturated with sodium chloride	Complete	Complete
5	0.1 N Oxalic acid saturated with sodium chloride	"	50%
6	Weakly acid (0.03 N H_2SO_4) 0.05 M solution of trilon saturated with sodium chloride	"	25%

The data in Table 2 show that the colored product of the (Cr^{IV} + DC) reaction formed an unstable complex with chromium ions and under certain conditions the chromium was extracted together with the colored compound. However, Table 2 also shows that the colored compound could also be extracted without chromium (experiments 3, 5 and 6). An investigation of the absorption spectra of the extracts showed that they were identical despite the chromium being partially or completely in the extract or almost completely remaining in the aqueous phase. Thus, the color of reaction product being studied depended on its own structure and not on coordination with chromium.

b) The Effect of Various Complex Formers. The colored solution obtained by the Cr^{VI} + DC reaction was treated with substances forming stable complexes with chromium ions. Trilon, oxalic acid and sodium fluoride were used as complex formers. In experiments with these complex formers there was no weakening in color as compared with control solutions even after long standing.

Experiments were also carried out in which the foreign complex former (trilon or oxalic acid) was added to a solution of diphenylcarbazide before the addition of potassium dichromate solution so that both of them could react with chromium ions at the moment when the latter were formed from chromate. Under these conditions the usual color always appeared. The colored compound was completely extracted with isoamyl alcohol in the presence of sodium chloride with approximately 50% (in the case of oxalic acid) or 75-80% of the chromium (in the presence of trilon) remaining in the aqueous phase (see Table 2, experiments 5 and 6).

For comparison one should note that the complex of mercury and DC was decomposed (the solution was decolorized) by the action of ions of chlorine and other elements. The complex of MoO_4^{2-} was decomposed by the action of an oxalic acid solution, etc. On the other hand, if an excess of bichromate solution was added, it decomposed the colored compound while the mercury – DC and molybden – DC complexes did not change in the presence of an excess of Hg^{2+} and MoO_4^{2-} ions. These experiments confirmed that the Cr^{IV} + DC reaction has a completely different character from the usual reactions of colored complex formation.

c) The Effect of Foreign Reducing Agents. If one assumes that the formation of a colored compound is based on the reaction of DC and DCO with di- or trivalent chromium ions at the moment when the latter are formed, then the presence of foreign reducing agents should evidently promote the formation of the colored compound. The following experiments were carried out. A solution of DC (as well as mixtures of DC and DCO) in 0.2 sulfuric acid was prepared. Stannous chloride, ascorbic acid or ferrous sulfate was added to the solution. A dilute solution of potassium dichromate was added to the mixture. In the presence of a foreign reducing agent there was either no color at all (with stannous chloride) or it appeared only at the point where the solution were combined, and weakened greatly on mixing. On changing the order of mixing, that is, when the reducing agent was added to a solution of potassium dichromate and the DC added immediately afterward, no color appeared at all. Besides this, it was established that on shaking a mixture of Cr^{III} and DC with zinc amalgam only a weak violet color appeared.

DISCUSSION OF RESULTS

The reaction of Cr^{VI} with DC is specific; no other oxidants (excluding MoO_4^{2-} etc.) form such colored compounds. It is therefore quite probable that in an intermediate stage in the reaction, complexes of DC with chromium of some intermediate valence are formed. With this, the DC is oxidized to form an intensely colored compound, probably of the quinhydrone type. This colored compound is capable of forming a complex with trivalent chromium although it can also be present in a solution unattached to the chromium and may even be separated from chromium without changing its color.

The data given still do not solve the nature of the Cr^{VI} and DC reaction completely. However, these data indicate that the reaction cannot be examined as a normal process of colored complex formation. The contradictions in the data of a number of authors are due to the different course of the extraction of chromium and the colored organic component, which depend on the acidity of the medium and salting-out effect of electrolytes (see Table 2).

SUMMARY

1. It was shown that trivalent chromium did not react with diphenylcarbazide or with diphenylcarbazone and that divalent chromium did not react with diphenylcarbazone. The incorrect data of a number of authors are explained by the occurrence of a side process, namely, the formation of a colored compound when acetic acid reacted with diphenylcarbazone (regardless of the presence or absence of chromium).

2. Cr^{VI} reacted with diphenylcarbazide to form a complex of trivalent chromium with the colored product of diphenylcarbazide oxidation. The colored product of the reaction of Cr^{VI} with diphenylcarbazide could be partially or wholly separated from chromium, depending on the conditons, with isoamyl alcohol and the absorption spectrum of the colored compound solution did not change.

3. It was shown that in the presence of foreign complex formers, the chromium combined with them, while the color of the solutions remained. In the presence of foreign reducing agents, no colored compound was formed in the reaction of Cr^{VI} with diphenylcarbazide.

4. Some problems in the chemistry of the Cr^{VI} + diphenylcarbazide reaction were discussed.

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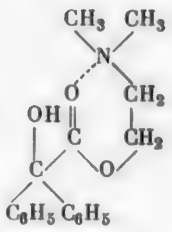
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SYNTHESIS OF CYCLIC AMINO ALCOHOLS WITH CHOLINOLYTIC PROPERTIES

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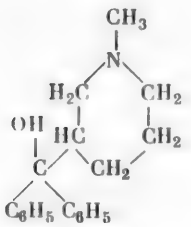
Previously, one of us [1] put forward the hypothesis that cholinolytic substances acting like atropine and belonging to the group of aminoalkyl esters of carboxylic acids interacted with cholinoreactive systems in an organism in a cyclic, fonic form, in which the separation between the nitrogen and the carbon atom attached to the cyclic radicals was fixed to a considerable extent due to intramolecular ion-dipole interaction and equalled approximately 3.7 A°. Here we present an example of such a cyclic structure for the case of the dimethylaminoethyl ester of benzilic acid.



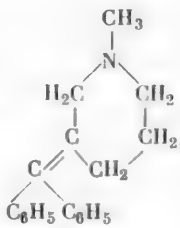
In this connection, the hypothesis naturally follows that a separation equal to 3.7 A° or comparatively close to it must correspond to the separation between some definite points of the cholinoreactive system and that it must exist in the molecule of the cholinolytic.

It seemed very desirable to find some sort of experimental confirmation of this hypothesis. For this purpose we planned the synthesis of cyclic structures similar to the one given but with a more rigidly set separation between the N and C due to the presence of a covalent bond instead of the comparatively weak ion-dipole one.

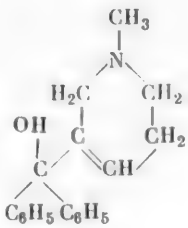
Below we present the structural formulas of such a series of cyclic compounds, whose synthesis we undertook.



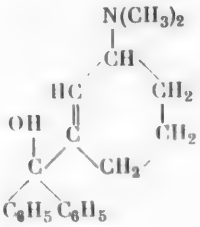
(I)



(II)



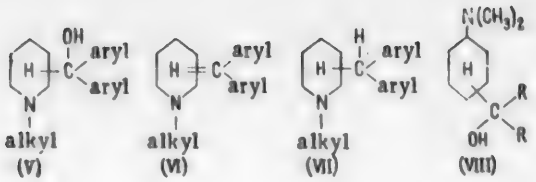
(III)



(IV)

(I) – 1-Methyl-3-diphenylmethylol-piperidine
(II) – 1-Methyl-3-diphenylmethylene-piperidine
(III) – 1-Methyl-3-diphenylmethylol-piperideine-3
(IV) – 3-Diphenylmethylol-dimethylaminocyclohexene-2

It should be noted that in the literature there are reports of the cholinolytic properties of a series of similar cyclic amino alcohols and amines. Thus, Sperber, Papa et al. [2-4] reported the spasmolytic and parasympathetic blocking activity of compounds with the general formulas (V), (VI) and (VII).



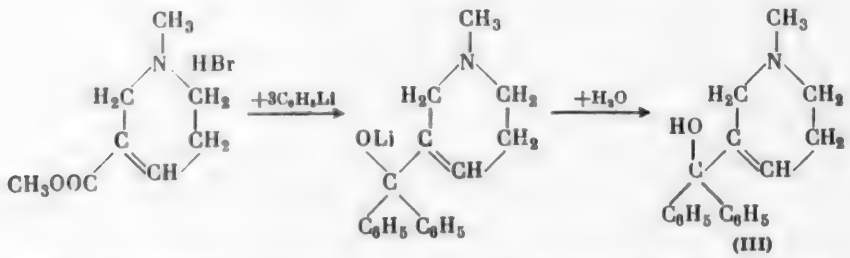
The substituting groups in these compounds may be in position 3 or 4 (rarely in position 2). The spasmolytic and parasympathetic blocking acitvities of compounds of the general formula (VIII) were reported by Villani [5] and Michajlyszyn [6].

However, the data presented in these papers did not make it possible to evaluate the cholinolytic activity of the given compounds quantitatively or to arrive at any conclusions on the problem interesting us. Moreover, only the first two of the substances that we planned to synthesize and investigate, namely (I) and (II), have been described in the literature. We were therefore obliged to synthesize all four of these compounds.

1-Methyl -3-diphenylmethylol-piperidine (I) was synthesized by one of the two methods described for it [3, 4, 7, 8], namely, by the action of phenyllithium on the methyl ester of 1-methylnipecotic acid.

1-Methyl-3-diphenylmethylene-piperidine (II) was obtained by dehydration of the previous compound analogously to the literature description [2-4]. As in the previous case, the hydrochloride and iodomethylate of this unsaturated amine were prepared.

We synthesized 1-methyl-3-diphenylmethylol-piperdeine-3 (III) for the first time. For its preparation, we chose the reaction of phenyllithium with arecoline.



The structure of the unsaturated amino alcohol obtained was confirmed by determining its molecular weight and also the nitrogen and active hydrogen content. Hydrogenation of the base (III) yielded the unsaturated amino alcohol (I).

Finally, 3-diphenylmethylol-dimethylaminocyclohexene-2, which has not been described in the literature either, was prepared by the following scheme:

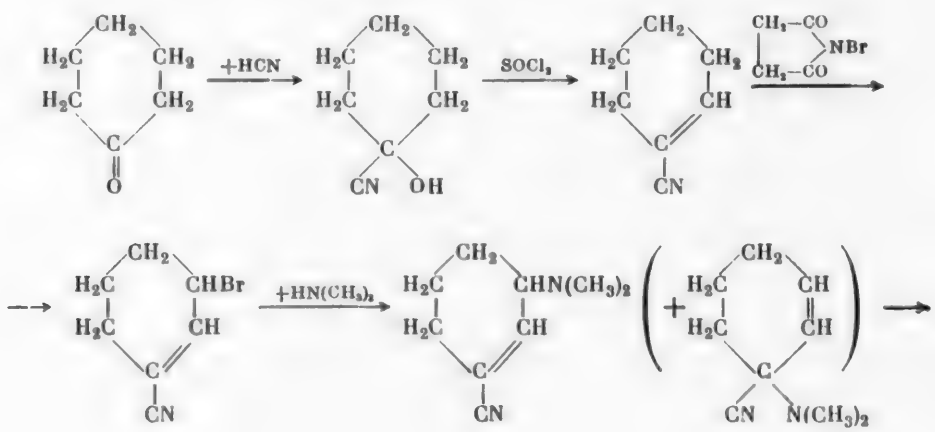


TABLE 1

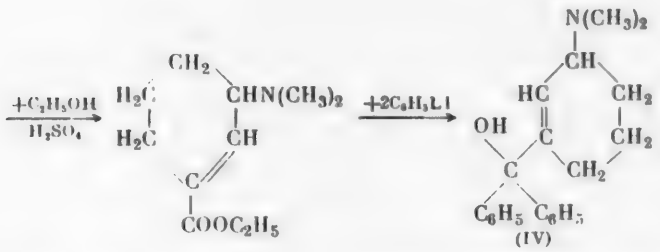
Cholinolytic Activity and Separation Between the N and C in the Molecules of the Hydrochlorides of the Substances Synthesized

Substance	Cholinolytic activity (dose in mg/kg)		Separation between N and C (in A°)
	peripheral	central	
(I)	100	> 150	3.0
(II)	70	80	3.8
(III)	17.5	17.5	3.9
(IV)	100	150	4.7

TABLE 2

Cholinolytic Activity and Separation Between the N and C in the Molecules of the Iodomethylates of the Substances Synthesized

Substance	Cholinolytic activity (dose in mg/kg)		Separation between N and C (in A°)
	peripheral	central	
(I)	12.5	> 100	3.9
(II)	80	–	3.8
(III)	5	> 100	3.8
(IV)	100	–	4.7



The first four stages of the synthesis were accomplished by methods described in the literature [9-11] with slight modifications in individual cases. Alcoholysis of the amino nitrile and interaction of the ethyl ester of 3-dimethylamino-1-cyclohexenecarboxylic acid, which was obtained for the first time, with phenyllithium were accomplished in analogy with known examples and led to the formation of the expected substances with the usual yields for these reactions.

The structure of the final reaction product, 3-diphenylmethylol-dimethylaminocyclohexene-2, was confirmed by determining its molecular weight and also by the nitrogen and active hydrogen contents. Hydrogenation of it gave 3-diphenylmethylol-dimethylaminocyclohexane, which has been described in the literature [6]. The hydrochloride of the unsaturated amino alcohol (IV) was obtained only in the form of an aqueous solution as it showed no tendency towards crystallization. Its iodomethylate was obtained in the crystalline state.

It should be noted that although the amination stage formed two isomeric amino nitriles, it was not necessary to separate the side product from the main one since the isomeric nitrile and its conversion products separated from the main product in the subsequent stages of the synthesis. For confirmation of this, we purified the amino nitrile through the picrate. The amino nitrile freed from isomers was subjected to the subsequent reactions. The product thus obtained was identical with the product obtained from the unpurified nitrile and the yields were not appreciably higher.

Starting from the most probable steric configurations and using molecular models of the substances synthesized, (I), (II), (III) and (IV), we calculated the separations between the nitrogen atoms and the carbon atoms attached to the phenyl radicals.

The cholinolytic activity of the substances obtained was determined by M. A. Razumova. It was determined on mice and expressed in doses of substance (in mg/kg) completely suppressing peripheral (salivation) and central (tremor) effects produced by arecoline. The data obtained for the hydrochlorides of substances (I), (II), (III) and (IV) are presented in Table 1 together with the calculated separations of the N and C.

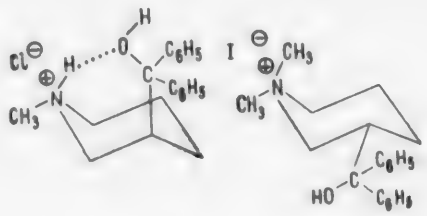
Examination of the data presented in Table 1 confirms the hypothesis on the existence of an effect on cholinolytic activity by the separation between the nitrogen atom of the cholinolytic substance and the carbon attached to the cyclic structures, whereby the most advantageous separation was actually close to 3.7 A° or slightly greater than this.

It is important to emphasize that all the substances compared differed little in molecular weight and three of them [(I), (III) and (IV)] contained the same functional groups, whose presence could be essential to their interaction with the cholinoreactive systems of the organism. Therefore, the difference in the cholinolytic activity of these substances must pertain, with a high degree of probability to the separation between these functional groups. It is characteristic that in going from substance (I) to (II), despite the disappearance of the hydroxyl group, which, as is known, strongly raises the cholinolytic activity, the latter not only did not fall, but even increased noticeably and this may be related to the increase in the separation between the N and the C from 3.0 to 3.8 A°. The introduction of a hydroxyl group into an analogous structure with the separation remaining close to 3.8 A° increased the cholinolytic activity even more as is seen on the example of substance (III).

With regard to substance (III), it is interesting to note yet another phenomenon. As was stated, it was synthesized by the reaction of phenyllithium with arecoline, a typical cholinomimetic substance. The substance obtained, containing the bulk of the arecoline structure, but "weighted" with two phenyl nuclei, was cholinolytic and antagonistic to arecoline.

On examining the properties of the iodomethylates presented in Table 2, attention is attracted by the considerable increase in the cholinolytic activity of the iodomethylate of compound (I) in comparison with that of its hydrochloride; in value it is similar to the activity of the iodomethylate of compound (III), although the hydrochlorides of the two bases differ strongly in activity.

The reason for this possibly consists in that the iodomethylate and the hydrochloride of (I) have different conformations. It is known that an axial disposition of a substituent produces greater steric hindrance than an equatorial one. However, in the case of the hydrochloride of (I) there is the possibility of an interaction between the oxygen of the hydroxyl group and the hydrogen at the nitrogen by a type of hydrogen bond, which is excluded in the case of the quaternary ammonium salt.



In addition, the presence of a second methyl at the nitrogen in the ammonium salt causes much greater steric hindrance to the diphenylmethylol group remaining in the axial position than the hydrogen in the case of the hydrochloride. It can therefore be stated with sufficient certainty that though the substituent occupies an axial position in the hydrochloride and the base, in the iodomethylate it is displaced to the less-hindered equatorial position, which involves an increase in the separation between the N and C from 3.0 to 3.9 A°. In its turn, this is advantageous as regards the activity of the preparation, since a separation of 3.9 A° is more favorable for interaction with the receptor than 3.0 A°.

EXPERIMENTAL

Methyl Ester of 1-Methylnipecotic Acid [12]. The iodomethylate of methyl nicotinate was hydrogenated in aqueous solution over a platinum catalyst (Adams's) at normal temperature and pressure. In all, about 95% of the theoretically required amount of hydrogen was absorbed over a period of 6-8 hours. Separation of the catalyst, neutralization, extraction, drying and distillation yielded about 80% of the theoretical amount of product, distilling at 84-85° (13 mm).

1-Methyl-3-diphenylmethylol-piperidine (I) [3, 7, 13]. With ice cooling, 3.84 g of methyl 1-methylnipecotate in 30 ml of ether was added to a solution of phenyllithium, obtained from 11.5 of bromobenzene, 1.08 g of lithium and 50 ml of absolute ether. The solution was then stirred for 1.5-2 hours at room temperature and then decomposed with ice. Glacial acetic acid (4 ml) was added to neutralize part of the alkali and the ether was removed by distillation. The residual light precipitate was separated from the water, washed and dried. The yield was 6.85 g (almost quantitative) and the m.p. 136-141°. Recrystallization from a mixture of benzene and ligroin yielded 5.28 g of pure product with m.p. 146.7-147.3°.

The hydrochloride was obtained by the action of an alcohol solution of HCl on an alcohol solution of the base. After recrystallization from alcohol, the substance melted with strong decomposition at 323°.

The iodomethylate was obtained by treating an acetone solution of the base with excess methyl iodide. When recrystallized from alcohol, it melted with decomposition at 267-268°.

1-Methyl-3-diphenylmethylene-piperidine (II) [2-4] (I) was dehydrated with dilute sulfuric acid according to literature data. The yield reached 95-97%.

After recrystallization from a mixture of alcohol and ethyl acetate, the hydrochloride melted at 249-250° (with decomp.).

Found %: Cl 11.82, 11.89. $C_{19}H_{22}NCl$. Calculated %: Cl 11.82.

The iodomethylate was recrystallized from a mixture of alcohol and ether; the m.p. was 210-212° (with decomp.).

Found %: I 31.44, 31.34. $C_{20}H_{24}NI$. Calculated %: I 31.31.

1-Methyl-3-diphenylmethylol-piperideine-3 (III). With cooling, 4 g of arecoline was added in one portion to a solution of phenyllithium, obtained from 1.10 g of lithium, 12 g of bromobenzene and 50 ml of absolute ether. The mixture was stirred vigorously and after a few minutes, a voluminous, light grey precipitate formed. The ice was removed and the mass stirred at room temperature for 1.5 hours. The flask was again immersed in an ice bath and the reaction mixture decomposed with ice and adjusted to a weakly alkali reaction (about 3 ml of glacial acetic acid). The ether was removed by distillation and the tarry solid residue separated and dried. The weight was 5.10 g. Recrystallization from toluene yielded 3.35 g (70.8%) of an almost colorless product with m.p. 187-188°. Subsequent recrystallization raised the melting point to 188.5-189.5°.

Found %: N 5.27, 5.22; OH 5.99, 6.29. Equiv. 284, 281. $C_{19}H_{21}ON$. Calculated %: N 5.01; OH 6.09. Equiv. 279.4.

The hydrochloride crystallized from an aqueous solution with one molecule of water and had m.p. 125-128° (with decomp.). It did not lose water on drying for many hours at 80° or in vacuum over P_2O_5. The salt was obtained in an anhydrous state only on drying above the melting point (130-135°).

Found %: Cl 10.57, 10.65; H_2O (cryst.) 5.55. $C_{19}H_{22}ONCl \cdot H_2O$. Calculated %: Cl 10.62; H_2O (cryst.) 5.38.

The anhydrous hydrochloride melted at 222.5-223° (with decomp.).

Found %: Cl 11.27, 11.19. $C_{19}H_{22}ONCl$. Calculated %: Cl 11.22.

After recrystallization from alcohol, the iodomethylate melted at 226.5-227° (with decomp.).

Found %: I 30.06, 30.17. $C_{20}H_{24}ONI$. Calculated %: I 30.13.

The iodoethylate was also recrystallized from alcohol. The m.p. was 218-218.5° (with decomp.).

Found %: I 29.43, 29.49. $C_{21}H_{26}ONI$. Calculated %: I 29.15.

Hydrogenation of 1-Methyl-3-diphenylmethylol-piperideine-3. 1 g of amino alcohol was hydrogenated over Adams's platinum catalyst (0.5 g) in glacial acetic acid. Over a period of 5 hours, about 95 ml of hydrogen (slightly more than the calculated amount) was absorbed. After removal of the catalyst and neutralization with ammonia, the product was extracted with chloroform. The chloroform was then removed and the residue recrystallized several times from a mixture of benzene and ligroin. The m.p. was 145.3-146.3°. A mixed melting point with 1-methyl-3-diphenylmethylol-piperidine was not depressed and a mixed melting point with the original unsaturated amino alcohol also was not depressed. However, authentic 1-methyl-3-diphenylmethylol-piperidine did not give a depression with 1-methyl-3-diphenylmethylol-piperideine-3.

The iodomethylate obtained from the hydrogenation product melted at 268-269° (with decomp.) and a mixed melting point with the iodomethylate of 1-methyl-3-diphenylmethylol-piperidine was not depressed.

Cyclohexene-1-cyanide. This substance was obtained by Ruzicka's method [9] in 48% yield.

3-Bromocyclohexene-1-cyanide. The cyclohexene was brominated in accordance with Mousseron's data [10, 11]. The yield of cyanide (calculated on the cyclohexene cyanide reacting) was 91.6%. A fraction boiling at from 125-141° (11 mm) was collected; the bulk of the material distilled at 132-138°.

3-Dimethylaminocyclohexene-1 Cyanide (and 3-dimethylaminocyclohexene-1 cyanide-3) [11]. About 30 g of dimethylamine was absorbed in 75 ml of benzene; with ice cooling, 22.6 g of bromocyclohexene cyanide was slowly added to the solution. On the following day the benzene and excess dimethylamine were removed by distillation and the residue diluted with water and made alkaline with sodium hydroxide. The alkaline solution was extracted with benzene several times and the extract dried with sodium sulfate. Distillation yielded 15.36 g (84.5%) of product.

B.p. 114-129° (13 mm), d_4^{20} 0.9674, $n^{20}D$ 1.4896, MR_D 44.70; calc. 44.85.

To free the 3-dimethylaminocyclohexene-1 cyanide from traces of isomer, the mixed amino nitriles were converted into the picrates. Fractional crystallization from alcohol yielded a fraction melting at 176.8-177.2°. Pure 3-dimethylaminocyclohexene-1 cyanide was obtained from this.

B.p. 125-129° (13 mm); d_4^{20} 0.9674, $n^{20}D$ 1.4909, MR_D 44.96; calc. 44.85.

Ethyl Ester of 3-Dimethylamino-1-cyclohexenecarboxylic Acid. 7.22 g of amino nitrile was dissolved in 12.5 ml of 95% ethanol and 9 ml of conc. H_2SO_4 added to the solution dropwise. The mixture was boiled for 13 hours. Ice was then added to the contents of the flask and the sulfuric acid neutralized with sodium carbonate. The oily layer which separated was extracted with chloroform. After drying with sodium sulfate and removal of the solvent, the residue was vacuum distilled. We obtained 5.6 g (59.5%) of a faintly greenish liquid, which distilled at from 107-119° (8 mm). During a second distillation, the whole product distilled over the same range.

d_4^{20} 1.0045, $n^{20}D$ 1.4800, MR_D 55.80; calc. 55.76.

3-Diphenylmethylol-dimethylaminocyclohexene-2 (IV). With ice cooling, 4.38 g of the ethyl ester of 3-dimethylamino-1-cyclohexenecarboxylic acid, dissolved in 40 ml of absolute ether, was added to a solution of phenyllithium obtained from 1.08 g of lithium, 10.5 g of bromobenzene and 50 ml of absolute ether. The ice bath was removed and the solution stirred for 2 hours at room temperature. The mass was then decomposed with ice and acidified and the ether removed by distillation. The aqueous solution was decanted from the tars liberated; it was treated with ether to remove the rest of the tars. After this, the aqueous solution was made alkaline and the tarry product extracted with chloroform. The extract was dried with sodium sulfate and the chloroform removed to leave 4 g of a brown oil, which rapidly crystallized. Recrystallization from a mixture of acetone and hexane gave 2.1 g (29.5%) of an almost colorless product with m.p. 136-137°. Subsequent recrystallizations raised the melting point to 137.5-138°.

Found %: N 4.85, 4.82; OH 5.83, 5.56. Equiv. 310, 308. $C_{19}H_{21}ON$. Calc. %: N 4.56; OH 5.53. Equiv. 307.4.

The hydrochloride could not be obtained in a crystalline state.

After recrystallization from alcohol, the iodomethylate melted at 185.5-185.7° (with decomp.).

Found %: I 28.40, 28.41. $C_{20}H_{24}ONI$. Calc. %: I 28.26.

Hydrogenation of 3-Diphenylmethylol-dimethylaminocyclohexene-2. 1 g of amino alcohol was hydrogenated over 0.5 g of Adams' platinum catalyst in ethanol solution at normal pressure and temperature. Somewhat more than the theoretical amount of hydrogen was absorbed over a period of 4 hours. After removal of the catalyst and the solvent, the residue was treated with ammonia and extracted with benzene, which was then removed by distillation. The residual tarry product could not be crystallized. The iodomethylate and hydrochloride were obtained from it directly.

The iodomethylate was recrystallized from alcohol. The m.p. was 235.5-242° (with decomp.).

Found %: I 28.14, 28.15. $C_{20}H_{26}ONI$. Calc. %: I 28.13.

The hydrochloride was recrystallized from a mixture of alcohol and ether and had m.p. 224-226° (with decomp.). The m.p. 243° is given in the literature [6].

Found %: Cl 10.14, 10.20. $C_{19}H_{24}ONCl$. Calculated %: Cl 10.23.

SUMMARY

1. We synthesized for the first time 1-methyl-3-diphenylmethylol-piperideine-3 and 3-diphenylmethylol-dimethylaminocyclohexene-2 and some of their salts and also the ethyl ester of 3-dimethylamino-1-cyclohexene-carboxylic acid, which was an intermediate product in the synthesis.

2. As a result of comparing the cholinolytic activity of the substances obtained with certain features of their molecular structures, we arrived at the conclusion that the separation between the nitrogen atom and the carbon atom attached to the cyclic radicals had an essential effect on the given physiological activity.

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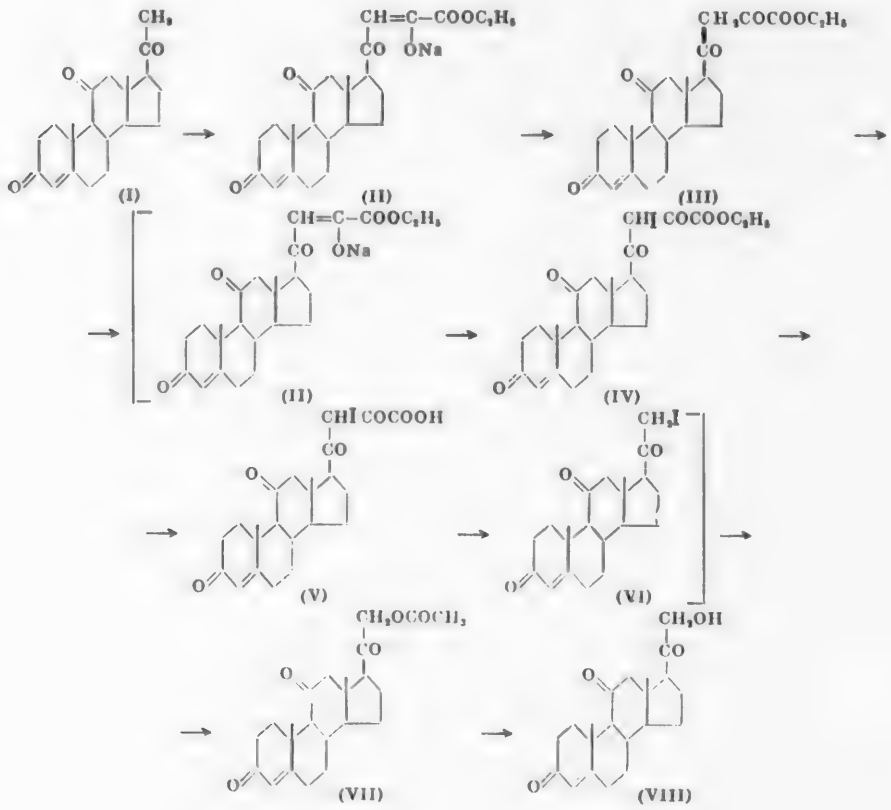
IV.* SYNTHESIS OF 11-DEHYDROCORTICOSTERONE FROM 11-KETOPROGESTERONE

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In an article by Hogg et al. [2] and in American patents [3, 4], the possibility of obtaining the acetate of 11-dehydrocorticosterone by condensation of 11-ketoprogesterone with diethyl oxalate were briefly discussed. The 21-ethoxyl derivative obtained was subjected to further conversions, as a result of which, the required product was obtained. It should also be noted that in papers on the synthesis of desoxycorticosterone acetate, Ruschig [5] described the condensation of diethyl oxalate with pregnenolone and Ercoli and Ruggieri [6] described a similar condensation with progesterone.

The article by Hogg did not give experimental data and the need to prepare 11-dehydrocorticosterone for pharmacological purposes and investigations led us to synthesize this compound from 11-ketoprogesterone by the following scheme:



*For our third article on this subject see [1].

11-Ketoprogesterone (I) was obtained by oxidation of an acetic acid solution of 11-α-hydroxyprogesterone [7] with chromic mixture. (I) was condensed with excess diethyl oxalate in benzene at room temperature with freshly prepared sodium methylate. For purification, an aqueous solution of enolate (II) was converted into the free ketoester (III) by treatment with dilute hydrochloric acid. By solution in methanol and treatment with the calculated amount of alcoholic sodium hydroxide, the ketoester (III) again gave (II). Iodination of (II) with iodine at -20° led to the iodine derivative (IV), which, without isolation, was subjected to hydrolysis with the formation of (V) and ketonic cleavage with the theoretical amount of sodium methylate in methanol at 0°. Replacement of the iodine in 21-iodo-11-ketoprogesterone (VI) by an acetoxy group by means of potassium acetate in acetone gave 11-dehydrocorticosterone acetate (VII). The technical (VII) was purified by means of grade "SKh" adsorbent and hydrolyzed to the free hormone (VIII) by our modification of Reichstein's method [8].

The total yield of 11-dehydrocorticosterone (VII) by the method developed was 41.4% (calculated on the 11-ketoprogesterone).

EXPERIMENTAL

Na-Enolate of 21-Ethoxalyl-11-ketoprogesterone (II). Into a three-necked flask, fitted with a mercury seal, a stirrer and a condenser, were placed 1.3 g of metallic sodium and 28 ml of anhydrous methanol. When the sodium had dissolved completely, 130 ml of anhydrous benzene was added, 80 ml of a mixture of solvents removed by distillation with careful heating and then 12 ml of diethyl oxalate and 17.15 g of 11-ketoprogesterone added at 35-40°. When the 11-ketoprogesterone was added, a gel-like precipitate of the sodium enolate formed immediately and the reaction mass acquired a yellow color. The mixture was stirred vigorously at room temperature for 2.5 hours, then 260 ml of dry ether added and stirring continued for 1 hour and finally a further 700 ml of dry ether added for complete separation of the product; after being stirred for another 1.5 hours, the light yellow precipitate was collected, washed with 100 ml of ether and dried in a vacuum desiccator over calcium chloride. The weight of the crude Na-enolate of 21-ethoxalyl-11-ketoprogesterone obtained was 23.1 g (98%).

Found %: C 69.77, 69.83; H 7.39, 7.46. $C_{25}H_{32}O_6$. Calculated %: C 70.07; H 7.54.

21-Ethoxalyl-11-ketoprogesterone (III). 23 g of crude Na-enolate of 21-ethoxalyl-11-ketoprogesterone (II) was dissolved in 600 ml of distilled water and the solution filtered. At room temperature and with stirring, a 5% solution of hydrochloric acid was added dropwise to the solution to an acid reaction to congo. The yellowish precipitate was collected, washed with water on the filter until neutral to litmus, pressed out well and dried in a vacuum desiccator over phosphorus pentoxide to constant weight. The weight of the precipitate was 22.0 g (98.1%, calculated on 11-ketoprogesterone).

21-Iodoethoxalyl-11-ketoprogesterone (IV) and 21-Iodo-11-ketoprogesterone (VI). 5 g of 21-ethoxalyl-11-ketoprogesterone was dissolved in 45 ml of methanol and to the solution at 0° was added 5.93 ml of 1.967 N sodium hydroxide in methanol dropwise with mechanical stirring. Over a period of 1.5 hours with stirring and cooling to -20°, a solution of 2.97 g of iodine in 70 ml of methanol was added to the solution of the Na-enolate of 21-ethoxalyl-11-ketoprogesterone formed. When all the iodine solution had been added, stirring was continued at -20° for a further 1.5 hours. The temperature was then raised to 0° and in the interval from 0° to -3°, the 21-iodoethoxalyl-11-ketoprogesterone was subjected to hydrolysis and ketonic cleavage without isolation. To the solution obtained (brown in color), 3.37 ml of a 3.4 N solution of sodium methylate in methanol was added dropwise with stirring over a period of 1 hour. Toward the end of the reaction, the solution became noticeably lighter and acquired a lemon-yellow color.

21-Iodo-11-ketoprogesterone was isolated by addition to a solution of 100 g of sodium chloride in 500 ml of water with stirring and cooling to 0°. The precipitate which separated was left to stand in the dark at room temperature for 6-10 hours and then the light yellow precipitate was collected, washed with water on the filter and rapidly dried in the dark in a vacuum desiccator over a fresh portion of phosphorus pentoxide. The weight of 21-iodo-11-ketoprogesterone obtained was 4.7 g (90%).

Found %: I 27.60, 27.57. $C_{21}H_{27}O_3I$. Calculated %: I 27.9.

11-Dehydrocorticosterone Acetate (VII). 6 g of 21-iodo-11-ketoprogesterone was dissolved in 300 ml of anhydrous acetone and 3.6 g of freshly fused potassium acetate was added to the solution. The mixture was heated to 60° with continuous stirring in a stream of nitrogen over a period of 7 hours. Then 150-160 ml of

solvent was removed in vacuum and the residue poured into 800 ml of ice water. The precipitate which formed was extracted with chloroform and the chloroform layer treated with 2% hydrochloric acid (cooled to 0°), 8% sodium bicarbonate solution and water to a neutral reaction to litmus and then dried over baked sodium sulfate. The chloroform solution was evaporated to dryness in vacuum at 40° and the residue dried for 2 hours in vacuum at room temperature. The substance required was extracted with 800 ml of a mixture of anhydrous acetone and ether (1:4). To the ether – acetone extract was added 25 g of "SKh" adsorbent and the mixture shaken for 1.5 hours. The adsorbent was removed by filtration, washed with 100 ml of ether – acetone mixture and 3 g of activated charcoal added to the combined filtrates. The mixture was shaken for another hour, the charcoal removed and washed with 25 ml of an acetone – ether mixture and the solution evaporated to dryness at 25-30° in vacuum. The yellowish residue of 11-dehydrocorticosterone acetate obtained was recrystallized from methanol. The weight was 3.2 g (62%). The white needles had m.p. 179-182°. $[\alpha]_D^{20}$ + 213° (acetone); λ_{max} 238 mμ; lgε 4.22.

The infrared spectrum of the 11-dehydrocorticosterone acetate contained the following absorption bands: 1745, 1700, 1644 and 1225 cm^{-1} (acetyl group).

11-Dehydrocorticosterone (VIII). To 0.7 g of 11-dehydrocorticosterone acetate was added 46.2 ml of methanol, 46.2 ml of water and 4.62 ml of conc. HCl. The mixture was boiled on a water bath with a reflux condenser for 50 minutes, quickly cooled to room temperature and poured into 500 ml of cold water containing 50 g of chemically pure sodium chloride. The reaction product was extracted 5-6 times with chloroform (total volume 850-900 ml) and the chloroform extract washed with 8% sodium bicarbonate solution and water to a neutral reaction to litmus and dried over anhydrous sodium sulfate. The sodium sulfate was removed, washed with dry chloroform and the filtrate combined. The chloroform solution was evaporated to dryness in vacuum with a water bath temperature of 40-45°. To the oily residue formed was added 15 ml of absolute ether; the product then precipitated in a crystalline form. The ether was removed completely by distillation and the yellowish crystalline residue of 11-dehydrocorticosterone recrystallized from butyl acetate. The yield was 0.47 g (75.8%). The m.p. was 174-178°. With the original 11-dehydrocorticosterone acetate the product gave a large depression of melting point.

Paper chromatography using the formamide – benzene system [9] (formamide, methanol 1:1) gave R_s = = 0.61. (11-α-Hydroxyprogesterone was used as the standard). Development with Lugol's solution gave an intense yellow color in contrast to 11-dehydrocorticosterone acetate, which gave a grey-green spot with the same developer.

The infrared spectrum of 11-dehydrocorticosterone contained the following absorption bands: 3380 (hydroxyl group), 1718, 1700 and 1664 cm^{-1}.

SUMMARY

A method was developed for preparing 11-dehydrocorticosterone by the scheme: 11-ketoprogesterone → → Na-enolate of 21-ethoxalyl-11-ketoprogesterone → 21-iodoethoxalyl-11-ketoprogesterone → 21-iodo-11-ketoprogesterone → 11-dehydrocorticosterone acetate – 11-dehydrocorticosterone.

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A NEW ALKALOID ISOMERIC WITH PLATYPHYLLINE

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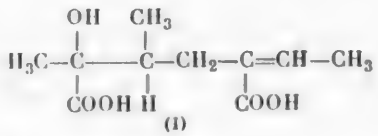
Platyphylline bitartrate is obtained from broad-leafed groundsel (Senecio platyphyllus). In chemical structure, platyphylline is the diester of platynecine and senecic acid [1].

During the treatment of the alcohol mother solutions under industrial conditions in the course of the isolation and recrystallization of platyphylline bitartrate, a new base was obtained which we called neoplatyphylline. Neoplatyphylline had the same over-all composition and the same functional groups as platyphylline; the infrared absorption spectra* (see figure) of these two bases were very similar and their basicities were identical. However, both neoplatyphylline and its salts differed in physical properties from platyphylline and the corresponding salts of the latter.

A pharmacological investigation of neoplatyphylline bitartrate showed that it had clearly expressed cholinolytic and spasmolytic properties. It produced dilation of the pupil and relaxed organs with smooth muscle. In the character of its action and activity, it was extremely similar to platyphylline but approximately twice as toxic as the latter. The alkaline and acid hydrolysis of neoplatyphylline yielded the same products as the degradation of platyphylline.

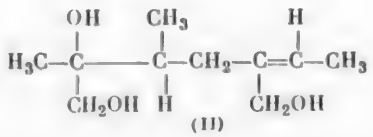
We surmised that the most probable reason for the difference in these two bases was a different steric configuration of the acid components in their molecules. As is known, necic acids with double bonds show geometrical isomerism besides optical isomerism [2].

Kropman and Warren [3] established that senecic acid had the structure of 2-hydroxy-3-methylheptene-5-dicarboxylic-2,5 acid (I).



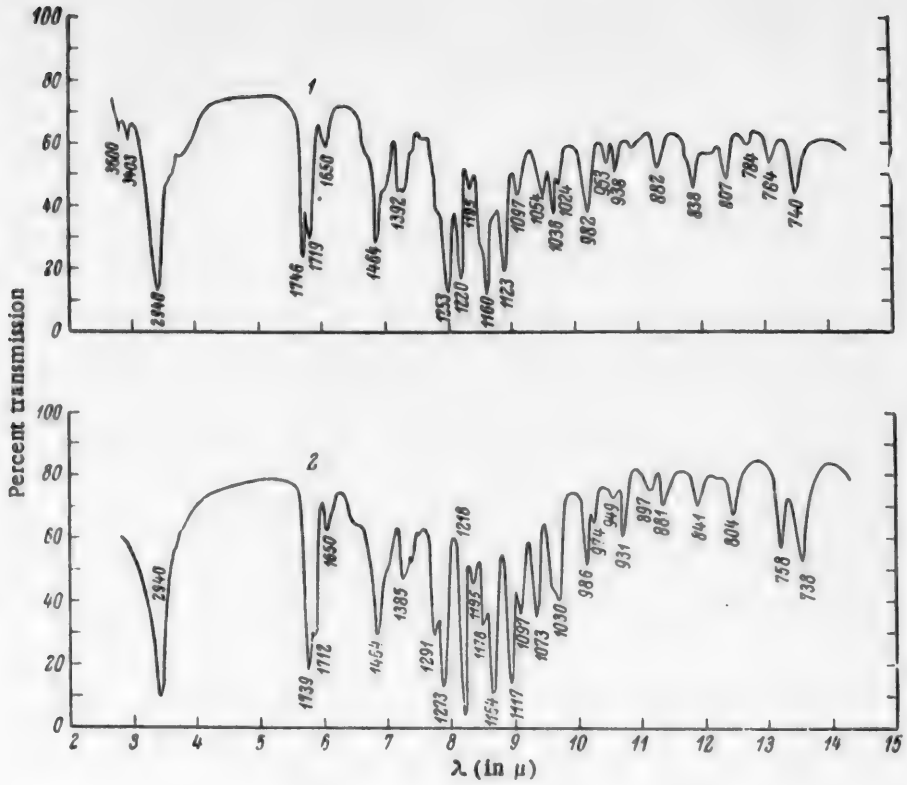
(I)

For further study of the properties of the acids esterifying platynecine in the molecules of neoplatyphylline and platyphylline, we reduced these alkaloids with lithium aluminum hydride. According to the structure of senecic acid proposed, the trihydric alcohols obtained as a result of the reduction should have the structure of 2-hydroxy-2,5-di-(hydroxymethyl)-3-methylheptene-5 (II).



(II)

*Plotted in the physicochemical laboratory of the All-Union Chemicopharmaceutical Scientific Research Institute under the direction of Yu. N. Sheinker.



Infrared-absorption spectra (in vaseline oil). 1) Platyphylline, 2) neoplatyphylline.

They were characterized as their p-nitrobenzoyl derivatives. The trihydric alcohol from neoplatyphylline formed a noncrystalline di-p-nitrobenzoyl derivative (A), which was optically inactive; the trihydric alcohol from platyphylline formed a crystalline di-p-nitrobenzoyl derivative (B), which had the same composition but was optically active ($[\alpha]_D$ + 19.41°).

It was interesting to study the properties of the trihydric alcohol obtained by reduction of senecic acid, formed by alkaline hydrolysis of both alkaloids. For this purpose, we prepared the dimethyl ester of senecic acid, which has not been described in the literature, and reduced it with lithium aluminum hydride. The trihydric alcohol obtained had the same composition but formed not a di-, but a mono-p-nitrobenzoyl derivative (C) with $[\alpha]^{20}D$ − 5.47°.

The results obtained confirmed our hypothesis that the reason for the difference between neoplatyphylline and platyphylline was a difference in the steric configurations of the esterifying acids. The fact that senecic acid which had undergone alkaline treatment formed a trihydric alcohol differing in properties from the alcohols obtained by direct reduction of the alkaloids confirmed our observation that necic acids isolated after hydrolysis of alkaloids from the Senecio genus with alkali had configurations which differed from those in which they existed in the alkaloid molecules.

EXPERIMENTAL

Isolation of Neoplatyphylline. The alcohol mother solution after isolation of platyphylline bitartrate and the separation of seneciphylline was concentrated to 1/4 of the original volume. The residue was cooled and the crystals of the bitartrate which separated were pressed out on a Buchner funnel and washed with alcohol. The m.p. was 175-180° (m.p. of platyphylline bitartrate 196°). The mixture of bitartrates obtained was dissolved in water, made alkaline with NH_4OH and the bases extracted with $CHCl_3$. Removal of the chloroform yielded a mixture of neoplatyphylline and platyphylline. For separation, the mixture was treated with an equal weight of CH_3OH at room temperature. The liquid was sucked from the insoluble neoplatyphylline and the solid product

washed with methanol and dried. The crude neoplatyphylline had protracted melting point (120-128°). After three recrystallizations from CH_3OH, the product had m.p. 131-133°; $[\alpha]^{20}D$ + 1.95° (c 10.20, $CHCl_3$); at a concentration of 3.79%, neoplatyphylline did not rotate the polarization plane. Neoplatyphylline was readily soluble in chloroform and acetone.

Found %: C 64.24; H 7.95; N 4.12. $C_{18}H_{27}O_5N$. Calculated %: C 64.09; H 8.01; N 4.15.

Neoplatyphylline Bitartrate. This substance was formed by mixing hot alcohol solutions of the base and tartaric acid (equimolecular amounts). After three recrystallizations from CH_3OH, the product had m.p. 138-140° (with decomp.), $[\alpha]^{20}D$ + 1.40° (c 10, water).

Found %: C 52.40; H 6.93; N 2.86. $C_{18}H_{27}O_5N \cdot C_4H_6O_6 \cdot H_2O$. Calculated %: C 52.27; H 6.93; N 2.77.

After being dried at 128° (0.03 mm) to constant weight, the product had m.p. 157-160° (with decomp.).

Found %: C 54.31; H 6.77; N 2.91. $C_{18}H_{27}O_5N \cdot C_4H_6O_6$. Calculated %: C 54.20; H 6.77; N 2.87.

Neoplatyphylline Perchlorate. The product had m.p. 217-218° (with decomp.) (from water).

Found %: C 49.27; H 6.39; N 3.26; Cl 8.20. $C_{18}H_{27}O_5 \cdot HClO_4$. Calculated %: C 49.37; H 6.40; N 3.20; Cl 8.10.

Neoplatyphylline Picrate. The substance had m.p. 164-165° (from alcohol).

Found %: C 50.70; H 5.33; N 10.05. $C_{18}H_{27}O_5N \cdot C_6H_3O_7N_3$. Calculated %: C 50.88; H 5.30; N 9.89.

Hydrolysis of Neoplatyphylline With Alcoholic KOH. 2 g of neoplatyphylline was heated on a water bath for 4 hours with 50 ml of a 0.5 N alcohol solution of KOH. The alcohol solution was evaporated to dryness. The residue was treated with dry chloroform. Removal of the chloroform yielded 0.75 g of an amino glycol with m.p. 147-148° (from acetone), $[\alpha]^{20}D$ − 60.30° (1.46, chloroform), which did not depress the melting point of platynecine. The residue after extraction of the platynecine with chloroform was dissolved in 3 ml of 10% HCl and extracted with ether. The ether solution yielded 0.8 g of an acid with m.p. 149-150° (from ethyl acetate) $[\alpha]^{18}D$ + + 10.40° (4.38, alcohol), which did not depress the melting point of the acid prepared by hydrolysis of platyphylline.

Hydrolysis of Neoplatyphylline With Hydrochloric Acid. 1 g of neoplatyphylline was boiled on a mantle with 20 ml of 17% HCl for 3 hours. The solution was cooled and treated with ether. Removal of the ether from the ether extract yielded 0.4 g of an acid with m.p. 151-152°, $[\alpha]^{18}D$ + 42.90 (c 4.29, alcohol). The acid did not depress the melting point of the lactone of senecic acid obtained by hydrolysis of platyphylline.

Reduction of Neoplatyphylline With Lithium Aluminum Hydride. 3 g of neoplatyphylline was dissolved in 600 ml of a mixture of absolute ether and absolute $CHCl_3$ (1 : 1). The mixture was boiled under reflux with stirring while 8 g of $LiAlH_4$ was gradually added. The reduction lasted for 16 hours. 100 ml of 10% H_2SO_4 was added to the cooled mixture dropwise. The layer of organic solvent was separated from the aqueous layer. The bulk of the trihydric alcohol (1.34 g) separated from the mixture of organic solvents as a thick, dark brown oil. The trihydric alcohol was purified by passing a chloroform solution through a column with Al_2O_3. The column was eluted with $CHCl_3$. The eluates yielded 0.5 g of a thick, slightly yellowish oil.

Preparation of Di-p-nitrobenzoyl Derivative (A). 0.5 g of the trihydric alcohol was dissolved in 5 ml of dry pyridine, 3 g of p-nitrobenzoyl chloride added and the solution left at room temperature for a day. Then 50 ml of water was added and the mixture extracted with ether. The ether solution was successively washed in a separating funnel with 10% H_2SO_4, water and $NaHCO_3$ solution and dried with Na_2SO_4. Removal of the ether yielded a noncrystalline p-nitrobenzoyl derivative as a thick, sticky substance. The substance was purified by passing a methanol solution through a column with Al_2O_3 and eluting with CH_3OH. Removal of the solvent from the eluates yielded a thick, colorless, noncrystalline oil, which dissolved readily in ether and chloroform and was difficultly soluble in alcohol and insoluble in water. It was dried at 100° and 0.03 mm pressure. The substance obtained did not rotate the plane of polarization at c 2.56 ($CHCl_3$).

Found %: C 59.63; H 5.56; N 5.71. $C_{24}H_{26}O_9N_2$. Calculated %: C 59.25; H 5.34; N 5.76.

Reduction of Platyphylline With Lithium Aluminum Hydride.* 3 g of platyphylline was dissolved in 800 ml of a mixture of absolute ether and absolute chloroform (1 : 1). The mixture was heated under reflux and

*Neither platyphylline nor neoplatyphylline were hydrolyzed when boiled with water or alcohol solutions of ammonia. Neither of these alkaloids were reduced by hydrogen in the presence of a platinum catalyst.

stirred while 8 g of $LiAlH_4$ was added. The course of the reduction process was checked by paper chromatography. The reduction process lasted for 24 hours. 100 ml of 10% H_2SO_4 was added dropwise to the cooled reaction mass with stirring. The organic solvent layer was separated from the aqueous layer. The solution was evaporated to dryness, and the weight of the residue was 1.08 g. The acidic aqueous layer was concentrated in vacuum, while the inorganic salts were removed as they separated by means of a Buchner funnel; the weight of the residue was 5.60 g. Both residues gave a positive reaction with silicotungstic acid. They were combined, dissolved in CH_3OH and passed through a column with espatite in the H-form. The column was eluted with CH_3OH and then with 5% ammonia in CH_3OH. The methanolic eluates yielded a mixture of trihydric alcohol with inorganic salts. Mixing with dry $CHCl_3$ yielded 0.43 g of thick, oily trihydric alcohol. The ammonia-methanol eluates yielded an oily substance giving a positive reaction for an alkaloid.

Preparation of Di-p-nitrobenzoyl Derivative (B) of the Trihydric Alcohol. 0.43 g of the trihydric alcohol was dissolved in 5 ml of dry pyridine, 2.12 g of p-nitrobenzoyl chloride added and the solution left at room temperature overnight. Then 50 ml of water was added and the mixture treated with ether. The ether solution was successively washed in a separatory funnel with 10% H_2SO_4, water and $NaHCO_3$ solution and dried with Na_2SO_4. The ether extract yielded 0.31 g of a crystalline substance. After four recrystallizations from anhydrous alcohol, the product had m.p. 136-137°, $[\alpha]^{18}D$ + 19.41° (c 2.06, $CHCl_3$).

Found %: C 59.53; H 5.37; N 5.92. $C_{24}H_{26}O_9N_2$. Calculated %: C 59.25; H 5.34; N 5.76.

Preparation of Dimethyl Senecate. 5 g of senecic acid with m.p. 146-147° and $[\alpha]_D$ + 10.3 was mixed with 25 ml of ether. To the mixture was added an ether solution of diazomethane (from 10.3 g of nitrosomethylurea) and the mixture left for 12 hours. Removal of the ether yielded 4.5 g of a colorless, oily, mobile substance. It had b.p. 113-114° (at 3 mm); $[\alpha]^{20}D$ − 16.88; d 1.0931.

Found %: C 58.81; H 8.40. $C_{12}H_{20}O_6$. Calculated %: C 59.01; H 8.19.

Reduction of Dimethyl Senecate With Lithium Aluminum Hydride. 3 g of platynecic ester was dissolved in 250 ml of absolute ether and 3.3 g of $LiAlH_4$ added gradually. The mixture was boiled under reflux for 5 hours. The mixture was cooled and 50 ml of 10% H_2SO_4 carefully added dropwise. The ether layer was separated from the aqueous one. The acidic aqueous layer was treated with ether. Removal of the ether from the ether extract yielded a slightly yellowish, thick oil; after being dried in a vacuum desiccator, the product weighed 2.60 g and had $[\alpha]^{20}D$ − 9.70 (c 2.18, $CHCl_3$).

Preparation of p-Nitrobenzoyl Derivative (C) of the Trihydric Alcohol. 1 g of alcohol, 10 ml of dry pyridine and 4 g of p-nitrobenzoyl chloride were left at 20° for 12 hours. The processing was as described above. Removal of the ether yielded 1.01 g of a slightly yellowish, viscous oil, which was insoluble in water. It was purified by passing a methanol solution through a column with Al_2O_3 (elution with CH_3OH). The substance did not crystallize after purification and drying; $[\alpha]^{20}D$ − 5.47° (c 6.21, $CHCl_3$).

Found %: C 60.97; H 6.68; N 4.30. $C_{17}H_{23}O_6N$. Calculated %: C 60.53; H 6.82; N 4.15.

SUMMARY

1. From the alcohol mother solutions from the isolation of platyphylline bitartrate, we isolated a new alkaloid isomeric with platyphylline, namely, neoplatyphylline.

2. The dimethyl ester of senecic acid was prepared and investigated.

3. The action of lithium aluminum hydride on platyphylline, neoplatyphylline and dimethyl senecate yielded trihydric alcohols, which have not been described in the literature and which had the same composition but different properties.

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SYNTHESES ON THE BASIS OF ANABASINE

XIII.* HYDROGENATION OF ANABASINE

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The hydrogenation of anabasine was accomplished for the first time by Smith [1]. He reduced synthetic DL-anabasine over a platinum catalyst in hydrochloric acid solution and obtained α,β'-dipiperidyl. Then Orekhov and Brodskii [2] hydrogenated natural anabasine (L-anabasine) with the help of Adams's catalyst and by Vishnegradskii's method and obtained a mixture of bases from which L-α,β'-dipiperidyl was isolated in the form of colorless crystals with m.p. 68-69° (in a sealed capillary) and $[\alpha]_D$ − 5°.

In their paper, Wenusch and Schöller [3] also described the reduction of L-anabasine (isolated from technical anabasine sulfate) in the presence of platinum − palladium black in glacial acetic acid. The base obtained was found to be identical with DL-α,β'-dipiperidyl.

In view of a certain interest in α,β'-dipiperidyl as the starting material for various syntheses and also for a more detailed study of the hydrogenation of anabasine, in the present work we attempted to find conditions for preparing α,β'-dipiperidyl from L-anabasine in higher yields.

For the hydrogenation of L-anabasine, we used a nickel catalyst prepared in the Organic Catalysis Laboratory of the Institute of Chemistry, Academy of Sciences, Uzbekh SSR and processed by Raney's method. The hydrogenation was carried out in an autoclave under a pressure of 105-110 atm at 100-130° in an aqueous medium and also without solvent.

Hydrogenation of L-anabasine without solvent formed crystalline DL-α,β'-dipiperidyl in 75% yield. After recrystallization, it had m.p. 51-59° and $[\alpha]_D$ ± 0°.

If L-anabasine was hydrogenated in aqueous solution or without solvent, but with the addition of a small amount of 10% sodium hydroxide solution, L-α,β'-dipiperidyl was obtained.

Attempts to hydrogenate anabasine hydrochloride in neutral and in hydrochloric acid media did not give positive results.

EXPERIMENTAL

Hydrogenation of Anabasine in Aqueous Solution. 32 g of L-anabasine in 100 ml of water was hydrogenated at 100-130° and 110 atm in the presence of 40 ml of catalyst. The hydrogenation was continued until a constant pressure was established in the autoclave. The solution obtained was then filtered free from catalyst and extracted first with ether and then with chloroform. The ether was distilled from the dried extract to yield 8.2 g of base with m.p. 50-56°. Treatment of the base with an alcohol solution of hydrogen chloride yielded a dihydrochloride, which did not melt when heated to 300°. $[\alpha]_D$ ± 0°. The DL-α,β'-dipiperidyl isolated from this dihydrochloride had m.p. 62-67°.

On vacuum distillation, the chloroform extract yielded 12.2 g of DL-α,β'-dipiperidyl with m.p. 110-115° (2 mm). The dinitroso derivative had m.p. 115-116°.

*For communication XII see J. Gen. Chem., 25, 1222 (1955).

Hydrogenation of Anabasine without Solvent. 128 g of L-anabasine was hydrogenated in the presence of 160 ml of catalyst at 110 atm and 100-125° to constant pressure in the autoclave. When unloaded from the autoclave, the reaction product rapidly solidified. For separation of the reaction product from the catalyst, it was dissolved in a mixture of alcohol and ether (1 : 1). After evaporation of part of the solvent and cooling, the solution deposited a crystalline precipitate of DL-α,β'-dipiperidyl with m.p. 51-59°. The dinitroso derivative had m.p. 116-117°.

After removal of the solvent, the mother solution was vacuum distilled. We obtained two fractions: 1st fraction, b.p. 120-130° (6 mm) – DL-α,β'-dipiperidyl and the 2nd fraction, b.p. 130-246° (6 mm) – a tarry mass. The DL-α,β'-dipiperidyl picrate had m.p. 219-220° (from alcohol).

Hydrogenation of Anabasine in Aqueous Solution with the Addition of Alkali. To 16.2 g of L-anabasine in 50 ml of water in an autoclave was added 20 ml of catalyst and 2-3 ml of 10% sodium hydroxide. The hydrogenation was carried out at 100-130° and 110 atm for 3 hours. The autoclave was filled with hydrogen three times and then the pressure in the autoclave remained constant. The reaction mixture was filtered free from catalyst and extracted with chloroform. On removal of the solvent and vacuum distillation, the extract yielded two fractions: 1st, b.p. 110-120° (5 mm), 13.1 g (78%), L-α,β'-dipiperidyl and the 2nd, b.p. above 120°, a tarry product (not investigated). L-α,β'-Dipiperidyl had m.p. 67-69°. Its picrate had m.p. 217-218° (from alcohol); $[\alpha]_D$ -5° (in alcohol).

Hydrogenation of Anabasine without Solvent with the Addition of Alkali. 64 g of L-anabasine was hydrogenated for 3 hours under a pressure of 105 atm at 100-130° in the presence of 80 cc of catalyst and 2-3 ml of 10% sodium hydroxide. The autoclave was filled with hydrogen until a constant pressure was established. The reaction mixture was treated with water and the solution freed from catalyst by filtration and extracted with chloroform. Removal of the $CHCl_3$ from the extract and vacuum distillation yielded two fractions: 1st b.p. 110-120° (5 mm), 47.1 g (73%), L-α,β'-dipiperidyl and the 2nd b.p. 120-130° (5 mm), 15 g, a tarry product. The picrate of the L-α,β'-dipiperidyl melted at 217-218° (from alcohol).

SUMMARY

1. A method was developed for hydrogenating anabasine in the presence of a nickel catalyst. The method made it possible to obtain α,β'-dipiperidyl in a yield of more than 75%.

2. It was established that the hydrogenation of L-anabasine in an aqueous medium and also without solvent formed inactive α,β'-dipiperidyl. The addition of a small amount of alkali made it possible to isolate active (levorotatory) α,β'-dipiperidyl.

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SEPARATION OF THE ALKALOIDS OF SOPHORA PACHYCARPA

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During the production of pachycarpine at the Chimkent pharmaceutical chemical factory, considerable amounts of high-boiling alkaloids from Sophora polycarpa have accumulated. These waste products contain known alkaloids, matrine and sophocarpine, which could be of independent interest as raw materials for synthetic investigations. In addition, this industrial concentrate could contain new bases, which could have been present in the plant itself in very small amounts so that they would be difficult to detect by a laboratory investigation of the plant.

A series of methods for the isolation of alkaloids from the plant Sophora pachycarpa is described in the literature [1-4]; a method is also known for the isolation of sophocarpine from the waste of the Chimkent pharmaceutical-chemical factory by means of ammonium chloride [5].

In continuing work on the study of the vat residue, accumulated in the production of pachycarpine from Sophora pachycarpa, we were able to develop a new method for separating the whole of the alkaloids, which is described in the present article.

The vat residue was a dark brown mass, which was soluble in water and organic solvents. It contained up to 8-10% of kerosine and moisture. By extraction and vacuum distillation, it was possible to obtain from it a fraction, which was a mixture of matrine and sophocarpine, and a difficultly distillable residue, representing about 40%.

To separate the mixture of sophocarpine and matrine we made use of the difference in their behavior with respect to potassium hydroxide. When treated with an alcohol solution of potassium hydroxide, matrine formed the potassium salt of matric acid while, while sophocarpine remained unchanged. Matrine could be obtained from the potassium salt of matric acid by the action of acetic anhydride on the latter.

In addition, we were able to separate a mixture of sophocarpine and matrine on the basis of the different solubilities of their N-oxides, which were formed by the action of hydrogen peroxide on the mixture of bases.

The N-oxide of sophocarpine, which has not been described in the literature, formed crystals with m.p. 68-69° and $[\alpha]_D$ + 36.2°. The N-oxide formed a picrate with m.p. 78-80° and a hydroiodide with m.p. 290°.

EXPERIMENTAL

Separation of a Matrine – Sophocarpine Mixture. 50 g of mixture (b.p. 161-230° at 5 mm) was heated with a solution of 20 g of potassium hydroxide in 200 ml of anhydrous alcohol for 4 hours under reflux. When the alcohol was partly evaporated, the solution deposited the potassium salt of matric acid in the form of colorless needles in 85.4% yield. The m.p. was 235-237° (from absolute alcohol).

Found %: N 9.13, 9.11. Equiv. 154.8, 155.75. $C_{15}H_{24}O_2N_2K$. Calculated %: N 9.21. Equiv. 152.

After separation of the potassium salt of matric acid, the alkaline solution was diluted with water and extracted with ether. Distillation of the residue from the ether extract yielded sophocarpine (b.p. 185-190° at 2 mm) with m.p. 74-75°. The yield was 13%.

Found M 245, 246. $C_{15}H_{22}ON_2$. Calculated M 246.

The hydroiodide (from anhydrous alcohol) had m.p. 272-274° (with decomp.).

Preparation of Matrine. To 10 g of the potassium salt of matric acid was added 50 ml of acetic anhydride. The mixture was heated on a water bath under reflux for 3 hours. The reaction product was then diluted with water, made alkaline with potassium carbonate and extracted with ether. On evaporation of the solvent, the matrine remained as a light yellow oil, which rapidly crystallized in air. The yield was 6 g. The m.p. was 75-76° (from ligroin). The matrine was identified by conversion to the potassium salt and the N-oxide of matrine. Matrine hydroiodide with m.p. 266-268° (from alcohol) was prepared.

Found %: I 33.5, 33.6. $C_{15}H_{24}ON_2 \cdot HI$. Calculated %: I 33.7.

Action of Hydrogen Peroxide on a Matrine – Sophocarpine Mixture. 30 g of the mixture was dissolved in 600 ml of 3% hydrogen peroxide solution and the solution left for 72 hours at room temperature. The solution was then evaporated under a water pump vacuum at 60-62° and the residue acidified with 15% hydrochloric acid and filtered. The filtrate was partially evaporated in vacuum, made alkaline with potassium carbonate and treated with chloroform. Distillation of the chloroform extract at normal pressure and then in vacuum at 40° yielded a thick, light yellow sirup, which was diluted with dry acetone to precipitate crystals of matrine N-oxide with m.p. 161-162° (with decomp.). The yield was 17.3 g. Matrine N-oxide was readily soluble in water and alcohol and difficultly so in acetone and ether. $[\alpha]_D$ + 45.36°.

Found %: N 9.98, 10.09. M 271, 270. $C_{15}H_{24}O_2N_2$. Calculated %: N 10.2. M 264.

The picrate had m.p. 214-216° (with decomp.; from anhydrous alcohol).

The mother solution after separation of the matrine N-oxide was evaporated to dryness in vacuum. To the residue was added 10 ml of anhydrous alcohol and a solution of hydriodic acid to an acid reaction to congo. During prolonged standing the hydriodide of sophocarpine N-oxide precipitated and had m.p. 290° (from a mixture of alcohol and acetone, 1 : 2).

Found %: I 32.35, 32.59. $C_{15}H_{22}O_2N_2 \cdot HI$. Calculated %: I 32.54.

3.6 g of the hydroiodide of sophocarpine N-oxide was dissolved in 5 ml of water. The solution was saturated with potassium carbonate and extracted with ether. The ether solution was concentrated to deposit sophocarpine N-oxide in the form of colorless crystals with m.p. 68-69° and $[\alpha]_D$ + 36.2°. Sophocarpine N-oxide was readily soluble in water, acetone, ether and benzene.

Found M 263, 264. $C_{15}H_{22}O_2N_2 \cdot HI$. Calculated M 262.

The picrate had m.p. 81-82° (from water).

Potassium Salt of Matric Acid N-oxide. 5 g of matrine N-oxide was dissolved in 30 ml of 15% alcohol solution of potassium hydroxide and the solution heated under reflux for 2 hours on a water bath. The solution was then evaporated to dryness in vacuum. The residue was recrystallized from a mixture of alcohol and acetone. The potassium salt of matric acid N-oxide precipitated in the form of colorless crystals with m.p. 195-197° (with decomp.). The yield was 3.2 g. The salt was readily soluble in water and alcohol and more difficultly soluble in acetone and ether. It titrated as a monoacidic base.

Found: equiv. 160.04, 156.5. $C_{15}H_{24}O_3N_2K$. Calculated: equiv. 159.5.

SUMMARY

1. A method was developed for separating a matrine – sophocarpine mixture by the action of an alcohol solution of potassium hydroxide.

2. The possibility of preparing matrine from the potassium salt of matric acid was demonstrated.

3. It was also shown that a matrine – sophocarpine mixture could be separated on the basis of the different solubilities of their N-oxides. The N-oxides of these bases were prepared and characterized for the first time.

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SULFURIC ACID METHOD OF SEPARATING THE ALKALOIDS OF ANABASIS APHYLLA

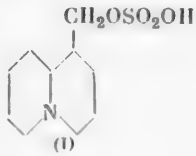
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A series of methods is known for the separation of the mixture of alkaloids from A. aphylla and these are based on differences in the physicochemical and chemical properties of the bases themselves and their derivatives [1].

In the present communication, a method is described which is based on the difference in the behavior of the alkaloids of this plant toward sulfuric acid. In some of our previous work [2] it was shown that the interaction of anabasine with strong sulfuric acid could be accomplished at a temperature of about 300°. Below 200°, a sulfo compound was formed, which readily decomposed under the action of alkali carbonates and hydroxides. To develop a method for separating the mixture of alkaloids with sulfuric acid, it was necessary to follow the behavior of the other alkaloids of A. aphylla toward this reagent.

In the first instance we studied the sulfonation of lupinine, which forms the bulk of the alkaloids associated with anabasine. The interaction of lupinine with concentrated sulfuric acid at room temperature and at 100° with various ratios of the reacting substances made it possible to establish that the reaction proceeded through the hydroxyl group with the formation of lupinine sulfate (I) in a yield of up to 60%. As can be seen from data in Table 1, the temperature conditions and excess acid only affected the yield of the ester. Lupinine sulfate formed crystals with m.p. 274-276°. It was readily soluble in water and difficultly so in methyl and ethyl alcohols; it did not dissolve in other organic solvents.



(I)

A study was then made of the conditions for hydrolysis of the ester by various reagents. The best results were obtained when the lupinine sulfate was hydrolyzed with 15% hydrochloric acid solution for 80-100 hours (Table 2). The different behavior of anabasine and lupinine toward sulfuric acid made it possible to separate the low-boiling mixture of alkaloids into individual bases (Table 3).

A study was then made of the interaction of sulfuric acid with other alkaloids of Anabasis (aphylline) aphyllidine etc.) at room temperature and at 100°. It was established that like anabasine, under these conditions they also gave readily decomposable sulfo compounds. This allowed us to develop a method of isolating anabasine and lupinine directly from anabasine sulfate (Table 4).

The method of isolating anabasine and lupinine from the total alkaloids of Anabasis could be realized in two ways. If barium carbonate was used for treating the sulfonation products, then the lupinine was isolated from the mixture in the form of the sulfate; alkali could be used, but in this case the properties of the sulfate hindered its isolation from the alkaline solution; therefore hydrolysis was necessary and then the lupinine was readily isolated in the form of the base.

Anabasine was isolated almost quantitatively from the mixture of alkaloids and lupinine in 50-60% yield.

EXPERIMENTAL

Lupinine Sulfate (I). With cooling, 1.5 ml of concentrated sulfuric acid (d 1.84) was added to 3.0628 g of lupinine (allowing 1.5 mole of sulfuric acid to 1 mole of lupinine). The reaction mixture was left for 12-14

TABLE 1

Sulfonation of Lupinine With Sulfuric Acid

Expt. No.	Reagents		Molar ratio of lupinine to H_2SO_4	Yield (in %)	Mother solution – residue after isolation of lupinine ester crystals (in g)
	lupinine (in g)	sulfuric acid (in ml)			
			At room temperature		
1	3.0628	1.5	1 : 1.5	32.21	1.5254
2	3.0324	2.0	1 : 2	42.47	1.2646
3	3.0036	3.0	1 : 3	53.92	1.2198
4	3.0270	4.0	1 : 4	60.54	0.6516
			At 100°		
1	3.0072	1.5	1 : 1.5	39.30	1.5278
2	3.0234	2	1 : 2	41.57	1.4108
3	3.0116	3	1 : 3	48.51	1.2594
4	3.0176	4	1 : 4	50.41	1.0648

TABLE 2

Hydrolysis of Lupinine Sulfate

Amount of ester (in g)	Concentration of reagents (in g)			Lupinine yield (in %)
	NaOH	HCl	H_2SO_4	
1.0	5	—	—	2.16
1.0	10	—	—	40.02
1.0	15	—	—	39.96
3.0	—	1	—	94.67
3.0	—	2	—	96.06
3.0	—	3	—	98.01
3.0	—	5	—	99.50
3.0	—	10	—	99.55
3.0	—	15	—	99.69
3.0	—	—	1	14.23
3.0	—	—	2	38.52
3.0	—	—	3	64.19
3.0	—	—	5	94.08
3.0	—	—	10	97.29
3.0	—	—	15	97.73

hours at room temperature and then dissolved in a small amount of water and treated with barium carbonate with heating. The filtrate after removal of the precipitate of barium carbonate and sulfate was evaporated to dryness and treated with methyl alcohol; this precipitated crystalline lupinine sulfate (1.4530 g, 32.2%) with m.p. 274-276°.

Found %: N 5.36, 5.56. M 240.1, 239.4. $C_{10}H_{19}O_4NS$. Calculated %: N 5.60. M 249.

The experiments on the preparation of lupinine sulfate at 100° differed only in that instead of standing at room temperature, the reaction mixture was heated for 8 hours at 100° (Table 1).

Hydrolysis of Ester. 3 g of lupinine sulfate in 20 ml of 1% hydrochloric acid was boiled for 10 hours. The solution was then made alkaline and extracted with ether. After removal of the solvent, the oil crystallized. We obtained 1.9268 g (94.7%) of lupinine with m.p. 67-68°.

TABLE 3

Separation of Anabasine – Lupinine Mixture

Reagents		Molar ratio of mixture to H_2SO_4	Yield of anabasine (in %)	Yield of lupinine sulfate (in %)	Weight of mother solution of residue (in g)	Yield of lupinine after hydrolysis of mother solution (in %)
anabasine–lupinine mixture (in g)	sulfuric acid (in ml)					
			At room temperature			
50.0	25	1 : 1.5	72.0	37.59	16.3720	—
50.0	32	1 : 2	93.86	37.15	13.1770	—
50.0	50	1 : 3	85.33	38.99	12.8660	—
50.0	66	1 : 4	71.0	21.90	9.2480	—
			At 100°			
50.0	25	1 : 1.5	88.00	22.79	10.9046	3.83
50.0	32	1 : 2	95.06	47.93	11.2554	3.47
50.0	50	1 : 3	97.88	31.61	12.9838	7.17
50.0	66	1 : 4	84.28	51.73	13.2892	3.09

TABLE 4

Isolation of Anabasine and Lupinine From Technical Anabasine Sulfate

Reagents – technical anabasine sulfate (in g)	H_2SO_4 (in ml)	Molar ratio of reagents	Yield of anabasine (in %)	Yield of lupinine sulfate (in %)	Mother solution (in g)	Yield of lupinine after hydrolysis (in %)
			At room temperature			
125	32	1 : 2	90.59	19.38	21.15	29.65
			At 100°			
125	32	1 : 2	88.28	11.84	14.94	40.96

Experiments on the hydrolysis of the sulfate in the presence of other concentrations of hydrochloric acid and corresponding concentrations of sulfuric acid and sodium hydroxide were carried out under the same conditions (Table 2).

Sulfonation of an Anabasine – Lupinine Mixture and Isolation of Anabasine. To 50 g of an anabasine – lupinine mixture was added 25 ml of concentrated sulfuric acid (d 1.84) with cooling (reagent ratio 1 : 1.5). The sulfonation mixture was left for 12-14 hours; it was then dissolved in 200 ml of water and boiled with barium carbonate. After removal of the mixture of $BaSO_4$ and $BaCO_3$ precipitates, the filtrate was extracted with chloroform. The solvent was removed from the extract and the residue vacuum distilled. We obtained 27 g (72%) of anabasine with $n^{15}D$ 1.5382 (Table 3). The aqueous solution was concentrated and treated with alcohol. This gave a crystalline precipitate of lupinine sulfate weighing 6.92 g (37.59%) and having m.p. 274-276°. The anabasine – lupinine mixture was separated with a larger excess of sulfuric acid under the same conditions. The experiments at 100° were carried out analogously to that described above, but instead of standing at room temperature the sulfonation mixture was heated for 8 hours.

Isolation of Anabasine and Lupinine From Technical Anabasine Sulfate. With cooling, 500 ml of sulfuric acid (d 1.84) was added to 1 kg of technical anabasine sulfate (1.5 mole of H_2SO_4 to 1 mole of anabasine). The reaction mixture was kept at room temperature for 18-20 hours (or heated on a water bath for 8 hours) and then dissolved in a small amount of water, made alkaline with 40% sodium hydroxide and exhaustively extracted with chloroform. The solvent was removed from the chloroform extract and the residue vacuum distilled. We obtained 348 g of anabasine and a certain amount of a mixture of high-boiling anabasis alkaloids. The aqueous mother solution was acidified with hydrochloric acid to a concentration of 15%. The acid solution was heated under reflux for 80-100 hours. The solution was then made alkaline and the lupinine extracted with chloroform. The solvent was distilled from the chloroform extract and the residue vacuum distilled. We obtained 43.15 g (70.16%) of lupinine with m.p. 67-68°. The residue was 7.5 g of tar, which distilled with strong decomposition.

The crystalline sodium sulfate which formed when the sulfonation mixture was decomposed with sodium hydroxide was separated and carefully washed with chloroform. After being dried, the chloroform extract was distilled. This made it possible to isolate a further amount of anabasine. The crystalline sodium sulfate which had been washed free from anabasine was dissolved in hydrochloric acid up to 15% concentration. The solution was boiled for 80-100 hours. Subsequent extraction with chloroform yielded a further amount of lupinine. Thus, on the whole, it was possible to isolate anabasine in 85-95% yield and lupinine in 65-70% yield (Table 4).

SUMMARY

A sulfuric acid method was developed for separating a mixture of anabasine alkaloids. The method was quite simple and could be quite applicable to the separation of alkaloids in laboratory practice.

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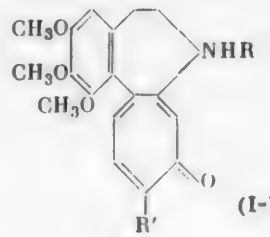
REMOVAL OF THE COLCHICINE ACETYL GROUP

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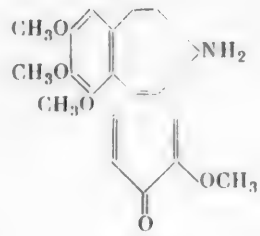
It is known that colchicine derivatives with more basic properties than colchicine itself (I) surpass it chemotherapeutically in a series of cases. Some of these are colchamine (II) [1, 2], which has been described in foreign literature under the names of "colchitine" [3], "alkaloid F" and "demecholcine" [4], desacetylcolchicine (III) [5] and aminocolchicide (IV) [6, 7].

On examining the formulas (I-IV), it becomes evident that an increase in the basic properties of colchicine may be achieved either by removal of the acetyl group or by replacement of the methoxyl of the tropone ring by an amino group.



(I-VI) and (VIII-X)

(I) R = $COCH_3$, R′ = OCH_3
(II) R = CH_3, R′ = OCH_3
(III) R = H, R′ = OCH_3
(IV) R = $COCH_3$, R′ = NH_2
(V) R = $COCH_3$, R′ = OH
(VI) R = H, R′ = OH
(VIII) R = $COCH_3$, R′ = SCH_3
(IX) R = H, R′ = SCH_3
(X) R = H, R′ = NH_2



(VII)

In the first instance, the action of hydrochloric acid on colchicine hydrolyzes the methoxyl group of the tropone nucleus and yields colchiceine (V) [8]. Subsequently, the acetyl group is removed to give desacetylcolchiceine (VI) (trimethylcolchicinic acid according to Zeisel). Colchiceine is normally obtained by the action of dilute acid. For removal of the acetyl group, the process was carried out in two stages with isolation of colchiceine and the use of comparatively concentrated acid in the second stage [8, 9]. One-stage processes for the preparation of desacetylcolchiceine recently began to be used [10-12]. We proposed a one-stage process with the use of 5% hydrochloric acid [12]. Below we present a simplified method for preparing desacetylcolchiceine from colchicine.

Consequently, the desacetylation of colchicine has been worked out completely. Unfortunately, the preparation of desacetylcolchicine by methylation of desacetylcolchiceine is difficult. As is known, methylation of the hydroxyl group of unsymmetrically substituted tropolones leads to the formation of two isomers [13]. This also occurs with the hydroxyl group of the tropolone ring of colchiceine [14] and desacetylcolchiceine. In the

latter case, the reaction products were desacetylcolchicine and isodesacetylcolchicine (VII) [10] and the latter did not have the required biological activity [15].

We attempted to find a method of removing the acetyl group of colchicine in such a way that the methoxyl group of the tropolone ring would be retained. It was previously reported that desacetylcolchicine could be obtained directly from colchicine by treating the latter with a solution of hydrogen chloride in anhydrous methanol [12]. Changing the experimental conditions did not lead to an improvement in yield. Further study showed that the process did not proceed in one stage, but was more complex and went through desacetylcolchiceine, which was methylated under the reaction conditions. The evidence of this reaction course was the following facts: 1) the presence of desactylcolchiceine in the reaction mixture was detected; 2) under the reaction conditions, it was possible to methylate desacetylcolchiceine and obtain desacetylcolchicine; 3) desacetylisocolchicine was detected in the reaction mixture by means of paper chromatography.

Under otherwise equal conditions, the amount of colchicine reacting and the yield of desacetylcolchicine changed in relation to the concentration of hydrogen chloride. In particular, at higher concentrations of hydrogen chloride, hardly any desacetylcolchicine was obtained and the bulk of the colchicine did not react. This fact also confirmed the reaction course presented above. It is known that a high concentration of hydrochloric acid in a mixture of alcohol, carboxylic acid and corresponding ester promotes esterification and not hydrolysis [16-18]. Therefore, in our case, at high hydrogen chloride concentrations the formation of desacetylcolchiceine was found to be limited; consequently, the formation of desacetylcolchicine was also limited. These observations again confirmed the presence of an analogy between esters and colchiceine ethers.

Removal of the acetyl group without touching the substituents of the tropolone ring has been achieved for certain colchicine derivatives. Thus, Velluz and Muller [19] found that hydrolysis of thiocolchicine (VIII) with an aqueous methanol solution of hydrogen chloride yielded desacetylthiocolchicine (IX).

We were able to hydrolyze aminocolchicide (IV) with dilute hydrochloric acid and obtained aminodesacetylcolchicide (X), which was characterized as the hydrochloride. Aminodesacetylcolchicide was obtained previously by other authors [10] starting from desacetylcolchicine. Analysis of the hydrochloride confirmed the over-all formula of aminodesacetylcolchicide as $C_{19}H_{22}O_4N_2$. Aminodesacetylcolchicide was a monoacidic base, as followed from the results of potentiometric titration and analysis data on the hydrochloride. The basicity must have been due to the amino group formed by deacetylation, though the amino group of the tropone ring also had weak basic properties. This conclusion follows in analogy with the properties of aminocolchicide. The latter forms a hydrochloride, which is readily decomposed by water. The weak basicity of the amino group of aminocolchicide also appeared in an attempt to determine its equivalent: in a back titration, the acid taken was titrated completely.

With aminodesacetylcolchidide, the basicity of the amino group of the tropone ring appeared when we took excess hydrochloric acid in the preparation of the hydrochloride; in this case the analysis for chlorine gave high results and the acidity of aqueous solution of the hydrochloride was considerably higher.

With a change in the concentration of the aqueous solution, the hydrochloride of aminodesacetylcolchicine changed the value of its specific rotation considerably. In a series of experiments carried out at temperatures from +17 to +22°, we found a linear dependence expressed by the formula:

$$[\alpha]_D = -[140\,(c - 0.22) + 200]^\circ, \ldots\ldots (1)$$

where c is the concentration in the range 0.350-0.700 g of substance/100 ml of solution.

We are very grateful to L. M. Utkin for his interest in this work.

EXPERIMENTAL

Desacetylcolchiceine (VI) (trimethylcolchicinic acid) From Colchicine. 49.5 g of colchicine, 100 ml of water and 100 ml of dilute hydrochloric acid (d 1.046) were heated on an oil bath in a round-bottom flask fitted with a stirrer and a reflux condenser. 2.3 mole of hydrochloric acid were taken for each mole of colchicine. The mixture was boiled for 6 hours. The colchiceine precipitate, which appeared at the beginning of heating, gradually dissolved. The solution was filtered to remove a small amount of impurities and evaporated on a water bath. Filtration and washing with the minimal amount of water yielded desacetylcolchiceine hydrochloride; the

weight was 44.61 g and the yield, calculated for a water of crystallization content of 1.75 moles [8], was 87.9%. Isolation of the desacetylcolchiceine and its recrystallization from methyl alcohol yielded 37.75 g of desacetylcolchiceine; the yield, calculated on a methyl alcohol of crystallization content of 2 moles, [20], was 74.8%; the m.p. was 157.2-158.8°, which is close to literature data [8, 10, 11]. In a series of experiments we isolated desacetylcolchiceine by precipitating it by neutralization of the acid solution; the yield of precipitated product, calculated on 2 moles of water of crystallization [8], was 84.9% and after recrystallization from methyl alcohol, 81.2%.

Desacetylation of Colchicine in a Methanol Solution of Hydrogen Chloride. In all the experiments, we used similar reaction mixtures: 5.0 ml of a solution of hydrogen chloride in anhydrous methanol was taken with 0.25 g of colchicine. After standing at room temperature, the mixture was diluted with water. The acid solution yielded a neutral fraction (A), a fraction of bases, which were insoluble in alkalis (B) and a fraction of bases, which dissolved in alkalis (C). Fractions (A) and (C) were recrystallized from ethyl acetate and methanol, respectively. We recovered colchicine and desacetylcolchiceine. In a series of experiments we limited ourselves to a qualitative reaction for desacetylcolchiceine. Fraction (B) was dissolved in alcohol and acidified with an alcohol solution of tartaric acid; desacetylcolchicine bitartrate crystallized on standing. The best results were obtained with a ratio of 10-25 moles of HCl per mole of colchicine. Increasing the length of the process from 5-6 to 10-15 days and more did not improve the yield appreciably, while the amount of colchicine recovered fell. With a considerable excess of hydrogen chloride (about 100 moles per mole of colchicine), the reaction hardly proceeded and 80-90% of the colchicine was recovered. In this case the presence of desacetylcolchiceine was not detected. The best yield of desacetylcolchiceine bitartrate was 0.03-0.04 g or 10-15% of theoretical, calculated on the colchicine reacting.

In one of the experiments, carried out under favorable conditions, it was shown that the mother solution after removal of the desacetylcolchicine bitartrate contained isodesacetylcolchicine. For this purpose, the base from the mother solution was chromatographed on paper. The R_f value was 0.27 (in two experiments). Simultaneously we found 0.27 and 0.29 for isodesacetylcolchicine and 0.21 and 0.20 for desacetylcolchicine. Ascending chromatography was used. The solvent system was isoamyl alcohol: water: acetic acid in the ratio 50:50:1.*

Action of Methanolic Hydrogen Chloride on Desacetylcolchiceine (VI). 1.0 g of desacetylcolchiceine, recrystallized from methanol, was dissolved in 20 ml of a solution of 1.065 g (about 12 moles) of hydrogen chloride in anhydrous methanol and left at room temperature. After 6 days, the acid solution was diluted with water and a fraction of bases, which were insoluble in alkalis (A), and a fraction of bases, which were soluble in alkalis (B), were isolated. Fraction (A) yielded 0.47 g of desacetylcolchicine bitartrate. The mother solution was shown to contain isodesacetylcolchicine: simultaneously with the above experiments, the R_f value was determined chromatographically and found to equal 0.29 and 0.30, respectively.

Desacetylaminocolchicide (X). 25.8 g of aminocolchicide was boiled for 4 hours in 110 ml of 10% hydrochloric acid. The cooled acid solution was washed with chloroform and made alkaline with excess 10% NaOH. The base liberated was extracted with chloroform. The extracts yielded 22.5 g of a tarry residue, which, according to titration, contained 77.1% of desacetylaminocolchicide, which represented a yield of 88.3%, considering that the original aminocolchicide contained 13.4% (0.5 mole) of chloroform of crystallization. The substance was dissolved in 35 ml of alcohol and 7.4 ml of an alcohol solution containing 1.85 g of HCl (calculated on 1 mole of HCl to 1 mole of amine) added. Yellow desacetylaminocolchicide hydrochloride crystallized on standing. After recrystallization from alcohol, it had m.p. 225-230° (with blackening). A mixture with desacetylaminocolchicide hydrochloride, obtained from desacetylcolchicine, melted without depression. The hydrochloride was readily soluble in water.

For ~0.5% solution at pH from 5.5 to 6.0. $[\alpha]_D^{20} - 222.0°$ (c 0.384), $[\alpha]_D^{21} - 234.0°$ (c 0.450), $[\alpha]_D^{23} - 265.1°$ (c 0.650). Calculated from formula (1): $[\alpha]_D - 223.0°, -232.2°, -260.4°$. For analysis, the substance was dried for 8 hours at 3 mm and 100°; weight loss 10.92%. $C_{19}H_{22}O_4N_2 \cdot HCl \cdot C_2H_5OH$. Calculated %: C_2H_5OH 10.85.

Found %: N 7.21; Cl 9.27. $C_{19}H_{23}O_4N_2Cl$. Calculated %: N 7.40; Cl 9.37.

On determining the carbon and hydrogen, it was not possible to obtain satisfactory results. Similar difficulties were reported for aminocolchicide and its N-derivatives [21].

*The paper was from the Leningrad factory. The chromatograms were developed with a modification of Dragendorf's reagent.

SUMMARY

1. A simplified procedure is presented for the preparation of desacetylcolchiceine from colchicine.

2. It was found that in the action of hydrogen chloride in methyl alcohol on colchicine, desacetylcolchicine was obtained by methylation of the initially formed desacetylcolchiceine.

3. It was found that aminodesacetylcolchicide could be obtained by boiling aminocolchicide with hydrochloric acid.

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INTERACTION OF AMMONIA WITH THE OXIDE OF PETROSELAIDIC ACID

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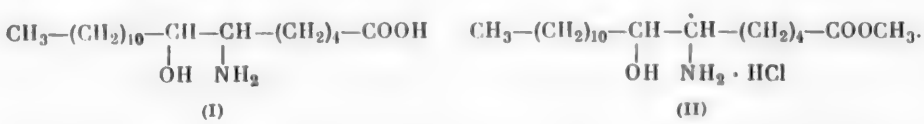
In a series of investigations [1], we showed that the interaction of oxides of higher unsaturated acids with ammonia led to the formation of hydroxy amino acids, whereby the hydroxyl group appeared in position removed from the carboxyl group. Oxides corresponding to stereoisomeric acids (cis- trans isomers), gave the corresponding stereoisomeric hydroxy amino acids. Two hydroxyaminostearic acids were thus synthesized from the oxides of oleic and elaidic acids. The oxide of petroselenic acid yielded 6-amino-7-hydroxyoctadecanoic-1 acid [2].

The present work is devoted to the study of the reaction of ammonia with the oxide of petroselaidic acid (trans-Δ6-octadecenoic-1 acid).

Petroselaidic acid with m.p. 53-54° was obtained by elaidation of petroselenic acid. Oxidation of petroselaidic acid with peracetic acid yielded the oxide with m.p. 66°. As a result of the interaction of ammonia with the oxide of petroselaidic acid at 130°, we isolated hydroxyaminostearic acid, which, after many recrystallizations from isoamyl alcohol, melted at 189-190° (in a sealed capillary) and had the composition $C_{18}H_{37}O_3N$ according to elementary analysis. The hydroxy amino acid was insoluble in the usual solvents, dissolved in amyl alcohol with difficulty and was soluble in alkalis and acids.

To prove the structure of the hydroxyaminostearic acid synthesized we used oxidation with lead tetraacetate, which we used quite successfully previously for similar purposes [3]. As a result of oxidation of the hydroxyaminostearic acid with m.p. 189-190°, we isolated lauric aldehyde, which was characterized as its semicarbazone with m.p. 102-103° [4] and 2,4-dinitrophenylhydrazone with m.p. 106° [5], and also a nitrogen-containing product, which gave adipic acid on hydrolysis. We therefore assumed that the hydroxyaminostearic acid with m.p. 189-190° which we obtained had the structure of 6-amino-7-hydroxyoctadecanoic-1 acid (I) and was a stereoisomer of the corresponding hydroxy amino acid obtained from petroselenic acid oxide.

We synthesized derivatives of the hydroxyaminostearic acid obtained from the oxide of petroselaidic acid: the hydrochloride of the hydroxy amino acid had m.p. 128-129° and the composition $C_{18}H_{35}O_3NH_2 \cdot HCl$ and the hydrochloride of its methyl ester (II) had m.p. 79-81°.



(I) (II)

It seemed of great interest to compare the properties of the stereoisomeric hydroxy amino acids we synthesized and their derivatives. From the data presented in the table we see that the melting points of the hydroxy amino acid and its derivatives, obtained from the oxide of petroselenic acid (cis-isomer) are lower than the melting points of the hydroxy amino acids and its corresponding derivatives, synthesized from the oxide of petroselaidic acid (trans-isomer).

Melting Points of Hydroxy Amino Acids and Their Derivatives

Name of compound	From petroselenic acid oxide [2]	From petroselaidic acid oxide
Hydroxyaminostearic acid	133—134°	189—190°
HCl salt of hydroxyaminostearic acid	81— 83	128—129
HCl salt of methyl ester of hydroxyaminostearic acid	--	79—81

We encountered a similar analogy on comparing the properties of two other hydroxyaminostearic acids, which we obtained from the oxides of oleic (cis-isomer) and elaidic (trans-isomer) acids, respectively [1].

In this and in the other case, the hydroxyamino acids differed from each other in steric configuration.

EXPERIMENTAL

Preparation of Petroselaidic Acid. 47 g of petroselenic acid was subjected to elaidination by Gold's method [6]. The petroselaidic acid obtained was recrystallized from anhydrous alcohol and had m.p. 53-54° and an iodine number of 87. The yield was 70%.

Preparation of Oxide. 33 g of petroselaidic acid was oxidized with peracetic acid in ether solution. As a result, we isolated an oxide, which had m.p. 66° after recrystallization from 70% alcohol [7].

Interaction of Ammonia With Oxide. We reacted ammonia with the oxide by the procedure we described previously [1]. The product obtained was purified by many recrystallizations from isoamyl alcohol and had m.p. 189-190° (in a sealed capillary). The yield was 38%.

Found %: C 68.21, 68.33; H 11.83, 11.80; N 4.48, 4.52. $C_{18}H_{37}O_3N$. Calculated %: C 68.52; H 11.82; N 4.44.

Oxidation With Lead Tetraacetate. 8.5 g of the hydroxyaminostearic acid was oxidized under the conditions described previously [3]. This yielded lauric aldehyde (74%) and a nitrogen-containing substance.

The semicarbazone of lauric aldehyde had m.p. 102-103°. A mixed melting point with a specially synthesized sample was not depressed.

Found %: N 17.44, 17.38. $C_{13}H_{27}ON_3$. Calculated %: N 17.45.

The 2,4-dinitrophenylhydrazone of lauric aldehyde melted at 106°.

Found %: N 15.45, 15.35. $C_{18}H_{28}O_4N_4$. Calculated %: N 15.39.

As a result of hydrolysis of the nonvolatile nitrogen-containing substance, we obtained adipic acid, whose presence was established by paper chromatography [8] (solvent — water-saturated butanol; reference — authentic adipic acid).

Preparation of Hydrochloride. 1.5 g of hydroxyaminostearic acid was treated with 7 ml of dilute hydrochloric acid containing 0.18 g of gaseous HCl. The salt was liberated immediately as a crystalline precipitate. After recrystallization from water and careful drying in a vacuum desiccator over solid KOH, the salt melted at 128-129°.

Found %: Cl 10.12, 10.12. $C_{18}H_{38}O_3NCl$. Calculated %: Cl 10.08.

Preparation of Hydrochloride of Methyl Ester. We described the preparation procedure previously [1]. The salt obtained was purified by recrystallization from ethyl acetate and appeared as fine needles with m.p. 79-81°.

Found %: Cl 9.46, 9.51. $C_{19}H_{40}O_3NCl$. Calculated %: Cl 9.69.

SUMMARY

1. Interaction of ammonia with the oxide of petroselaidic acid yielded 6-amino-7-hydroxyoctadecanoic-1 acid with m.p. 189-190°, which was stereoisomeric with the hydroxy amino acid synthesized from the oxide of petroselenic acid.

2. The hydrochloride of 6-amino-7-hydroxyoctadecanoic-1 acid with m.p. 128-129° and the hydrochloride of its methyl ester with m.p. 79-81° were synthesized.

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STUDY OF ALKALOIDS OF THE C_{15} SERIES

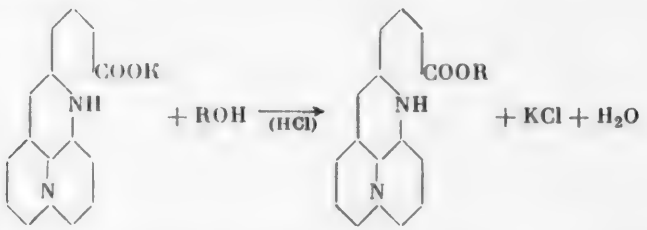
II. THE ESTERS OF MATRIC ACID

A. S. Sadykov and Ya. I. Pakanaev

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In the previous articles [1], reports were given on new methods of isolating matrine and matrine N-oxide from the vat residues from the production of pachycarpine at the Chimkent chemical pharmaceutical factory and also on sophocarpinols.

In the present paper we present the results of synthesizing esters of matric acid, starting from the potassium salt of matric acid and appropriate alcohols by the scheme:



The reaction was accomplished by passing dry hydrogen chloride into a solution of the potassium salt of matric acid in the appropriate alcohol [2]. The unreacted alcohol was removed by distillation and the residue made alkaline with 35% sodium hydroxide and extracted with ether. Removal of the solvent left crystalline esters of matric acid.

In this way we synthesized the methyl, ethyl, propyl, isopropyl, butyl, isobutyl, amyl and benzyl esters of matric acid. They were colorless, crystalline substances, which dissolved readily in water and the usual organic solvents and with more difficulty in ligroin. The methyl, ethyl, butyl and benzyl esters distilled in vacuum and did not change during long storage. All the ester titrated as monoacidic bases.

The properties of the esters synthesized are presented in the table.

EXPERIMENTAL

Isobutyl Ester of Matric Acid. Into a solution of 5 g of the potassium salt of matric acid in 50 ml of anhydrous isobutyl alcohol was passed hydrogen chloride for 2 hours. A few minutes after the passage of hydrogen chloride began, the whole of the potassium salt of matric acid precipitated as the hydrochloride, which gradually dissolved as more hydrogen chloride was passed. At this, the solution evolved a considerable amount of heat; the mixture was cooled with water. At the end of the reaction, potassium chloride precipitated to the bottom of the flask and was removed by filtration. The alcohol solution was evaporated to dryness in vacuum. The hydrochloride thus obtained was found to be a strongly hygroscopic substance. It was dissolved in 10 ml of water and transferred to a separatory funnel. With cooling, 100 ml of ether and 15 ml of 35% sodium hydroxide were poured in and a considerable amount of potash was added until a paste formed. After vigorous shaking, the ether solution was poured off and the residue again extracted with ether (3 × 50 ml). The combined ether extracts were filtered and

Esters of Matric Acid

Name	Empirical formula	Yield (in %)	Melting point	Analysis data on nitrogen (in %)		Melting point of derivatives		
				found	calculated	picrate	iodoethylate	hydroiodide
Methyl	$C_{16}H_{28}O_2N_2$	46.2	79°	10.11, 10.32	10.0	105—106°	—	—
Ethyl	$C_{17}H_{30}O_2N_2$	63	75—76	9.23, 9.54	9.52	94	283—284°	—
Propyl	$C_{18}H_{32}O_2N_2$	62	60	9.27, 9.0	9.09	57	—	—
Isopropyl	$C_{18}H_{32}O_2N_2$	33	61	8.86, 9.27	9.09	86	270—271	—
Butyl	$C_{19}H_{34}O_2N_2$	40.2	73	8.62, 8.70	8.69	116	—	279°
Isobutyl	$C_{19}H_{34}O_2N_2$	52	195—196	8.72, 8.58	8.69	113—114	—	--
Amyl	$C_{20}H_{36}O_2N_2$	53.1	148	8.35, 8.12	8.33	96— 98	—	—
Benzyl	$C_{22}H_{32}O_2N_2$	41	68	7.91, 7.78	7.83	102—103	—	265—266

dried with potassium carbonate. Removal of the solvent left colorless crystals of the isobutyl ester of matric acid with m.p. 195-196°. The yield was 2.6 g (52%).

The other esters were synthesized similarly.

SUMMARY

Starting from the potassium salt of matric acid and the appropriate alcohols, we synthesized the methyl, ethyl, propyl, isopropyl, butyl, isobutyl, amyl and benzyl esters of matric acid.

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INVESTIGATION OF ACONITUM NEMORUM ALKALOIDS

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Of the Catenata section of the Aconitum genus, to which Aconitum nemorum M. Pop. (Wood Aconite) belongs, A. talassicum [1, 2] and A. soongoricum [3, 4] have been investigated previously. Alkaloids of the atisine group were found in both plants.

As material for our investigations we used the above-ground parts and the roots of A. nemorum, collected in the mountains of the Zailiisk Ala-Tau (in the neighborhood of N. Turgen', Alma-Ata district) at various phases of the plant's growth. The alkaloid contents of the different organs were not the same [5] and varied considerably, depending on the time of gathering. The maximum amount of alkaloids (up to 2.18%) accumulated in the roots toward the end of the plant's growth.

The bulk of the total alkaloids in all the plant samples we investigated consisted of a new alkaloid named nemorine. The alkaloid gave a readily crystallizable oxalate, tartrate and picrate; crystalline salts were not obtained with mineral acids. Elementary analysis of nemorine in conjunction with the molecular weight, determined both by titration and by the cryoscopic method, led to the formula $C_{24}H_{39}O_4N$. In attempts at hydrogenation with a platinum catalyst, the nemorine was recovered unchanged. In agreement with this, the UV absorption spectrum of the alkaloid (in heptane) and its hydrochloride (in water) showed no absorption maxima in the range 220-360 mμ, which is characteristic of double bonds. The Zerevitinov-Chugaev method showed that nemorine contained two free hydroxyl groups. In a reaction with acetyl chloride, one of these was acetylated with the formation of O-acetylnemorine. The other two oxygen atoms were present in the form of methoxyl groups. When heated with hydriodic acid, the two latter were readily hydrolyzed to give a compound with the composition $C_{22}H_{33}O_3N$, which was named aponemorine in analogy with apomorphine. Apparently, in addition to hydrolyzing the methoxyl groups, hydriodic acid simultaneously reduced one of the existing or free hydroxyl groups. Nemorine was recovered unchanged from a reaction with methyl iodide in methanol solution. For determination of the character of the N-alkyl group, the nemorine was oxidized with potassium permanganate. This yielded acetaldehyde, indicating that an ethyl group was attached to the nitrogen in the nemorine molecule.

All this indicated that the formula for the nemorine molecule could be expanded to the following form: $C_{22}H_{26}(OH)_2(OCH_3)_2NC_2H_5$.

EXPERIMENTAL

Isolation of alkaloids. 20 kg of dry, powdered roots of wood aconite (gathered in autumn) were wetted with 20% sodium carbonate solution and exhaustively extracted with chloroform. The alkaloids were extracted from the chloroform solution first with 10% and then with 5% sulfuric acid. The solutions were made alkaline with sodium bicarbonate and the alkaloids extracted with chloroform. Removal of the solvent left 43.6 g of total alkaloids, representing 2.18% of the weight of the original raw material.

For separation, the total alkaloids were dissolved in 1% H_2SO_4 and fractionally extracted: firstly (without being made alkaline) with chloroform, secondly (after the addition of sodium acetate) with ether and thirdly (after being made alkaline with sodium carbonate), exhaustively with chloroform. Paper chromatography (system: n-butanol – water – acetic acid 10 : 4 : 1; developer – Dragendorf's reagent) showed that the first fraction contained

two substances (R_f 0.80-0.84, 0.72-0.74), the second, three (R_f 0.72-0.74, 0.59-0.60, 0.49-0.51) and the third, one (R_f 0.59).

We investigated the third fraction, which was greatest in amount (30.0 g) and consisted of strong bases. It was repeatedly treated with hot ligroin. The solution obtained was filtered and concentrated to small volume. On standing, this solution deposited a dark yellow crystalline precipitate of nemorine.

Similarly, the leaves collected in autumn yielded 0.28% of total alkaloids (according to the data of Yunusov [3], the above-ground part of A. nemorum contains 0.26% of alkaloids), including 0.07% of nemorine. Paper chromatography established that the above-ground organs of the plant contained the same substances as the roots.

Nemorine. The crude alkaloid was recrystallized from aqueous acetone and then many times from methanol. Nemorine was deposited from methanol solution in the form of elongated prisms with m.p. 126-128°, $[\alpha]_D^{17}$ – 4.5 ± 1° (c 4.16, ethanol). Nemorine was readily soluble in ether, chloroform, benzene, acetone and ethyl and methyl alcohols and difficultly soluble in water (1 : 1000).

Found %: C 71.23, 71.25; H 9.97, 9.93; N 3.56; OCH_3 14.91, 15.19; H (active) 0.44, 0.40 Equiv. 417.80, 411.85 (acidimetry). M 407.17 (by Rast's method). $C_{24}H_{39}O_4N$. Calculated %: C 71.07; H 9.69; N 3.45; $2OCH_3$ 15.30; 2H (active) 0.50. M 405.58.

Nemorine oxalate was obtained by mixing acetone solutions of the alkaloid and oxalic acid. After recrystallization from acetone, the acid oxalate of nemorine melted at 175-176°. Nemorine oxalate was readily soluble in methanol, ethanol and acetone.

Found %: C 61.12, 61.25; H 8.10, 7.98; N 2.67, 2.77; H_2O 3.36. $C_{24}H_{39}O_4N \cdot C_2H_2O_4 \cdot H_2O$. Calculated %: C 60.80; H 8.44; N 2.73; H_2O 3.51.

Nemorine tartrate was obtained by mixing an alcohol solution of tartaric acid with an acetone solution of the alkaloid. After recrystallization from anhydrous alcohol, the salt had m.p. 162-163°.

Nemorine picrate was formed by mixing alcohol solutions of nemorine and picric acid. After recrystallization from anhydrous alcohol, the picrate melted at 105-106°.

O-Acetylnemorine. 2.0 g of nemorine in 30 ml of acetyl chloride was left to stand in a sealed tube for 13 days. The oil which formed after evaporation of the excess acetyl chloride was dissolved in water. The solution was neutralized with ammonia and the base extracted with ether. After many days standing, the ether solution (evaporated to small volume) deposited rhombic crystals. After recrystallization from ether, the O-acetylnemorine had m.p. 110-113°.

Found %: C 69.95, 69.68; H 9.01, 9.39; N 2.98, 3.00. Equiv. 454.50 (acidimetry) $C_{26}H_{41}O_5N$. Calculated %: C 69.77; H 9.23; N 3.13. M 447.62.

Determination of N-alkyl Group. Over a period of an hour, 10 ml of 5% aqueous potassium permanganate solution was added dropwise to an ice-cooled solution of 1.0 g of base in 5 ml of 1 N sulfuric acid. The aldehyde thus cleaved was condensed with dimedone in the usual way [2, 3]. The crystals obtained had m.p. 135-137° and did not depress the melting point of the product from the condensation of acetaldehyde with dimedone.

Aponemorine. A solution of 2.0 g of nemorine in 8 ml of hydriodic acid (d 1.7) was heated for an hour at a bath temperature of 130-135° until the methyl iodide had distilled completely. The cooled solution was neutralized with ammonia and the base extracted with ether. The extract was dried with potassium carbonate, and the ether removed to yield 1.8 g of a substance, which had m.p. 168-170° after many recrystallizations from methanol. Aponemorine was readily soluble in methanol, ethanol, chloroform and ether.

Found %: C 73.37, 73.90; H 9.05, 9.26; N 4.04, 4.08. $C_{22}H_{33}O_3N$. Calculated %: C 73.50; H 9.25; N 3.90.

SUMMARY

A new alkaloid, nemorine, with the composition $C_{24}H_{39}O_4N$ was isolated from wood aconite (Aconitum nemorum M. Pop.). From a determination of the functional groups, a partially expanded formula of nemorine is given: $C_{20}H_{26}(OH)_2(OCH_3)_2NC_2H_5$.

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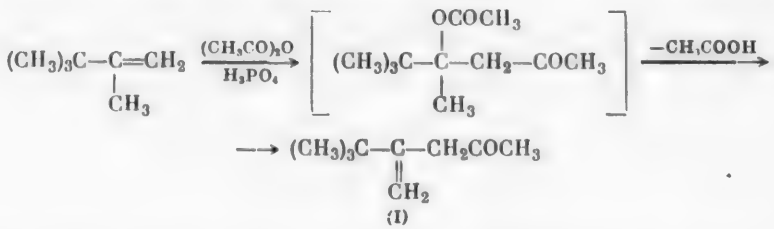
LETTERS TO THE EDITOR

PHOTOCHEMICAL ISOMERIZATION OF VINYL KETONES TO ALLYL KETONES

R. Ya. Levina, V. N. Kostin and P. A. Gembitskii

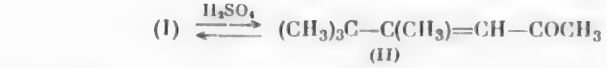
Moscow State University

The acylation of tryptene (2,2,3-trimethylbutene-3) with acetic anhydride in the presence of phosphoric acid led to the formation of an unsaturated ketone with a double bond in the β,γ-position with respect to the carbonyl group, namely, 2,2-dimethyl-3-methylenehexanone-5 (I).



(I)

On standing for several months, ketone (I) isomerized with transposition of the double bond to 2,2,3-trimethylhexen-3-one-5 (II); this formed an equilibrium mixture of the original ketone (I) and its isomerization product (II).

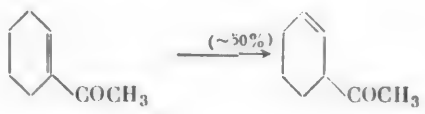


(II)

If the equilibrium mixture of isomeric, unsaturated ketones obtained was irradiated in quartz with ultraviolet light, then its α,β-form, the vinyl ketone (II), isomerized completely into the original β,γ-form, the allyl ketone (I): (II) → (I).

Thus, from a mixture of α,β- and β,γ-unsaturated ketones there was formed pure β,γ-unsaturated ketone, 2,2-dimethyl-3-methylenehexanone-5.

Wishing to determine whether this photochemical isomerization of vinyl ketones into allyl ketones had a general nature, we also irradiated 1-acetylcyclohexene-1 with ultraviolet light; it was found that 1-acetylcyclohexene-1 was approximately 50% isomerized to 1-acetylcyclohexene-2.



Thus, vinyl ketones are isomerized photochemically* (partially or completely) to allyl ketones.

*It is known that vinyl ketones are isomerized to allyl ketones under the action of acids and alkalis [1].

EXPERIMENTAL

Acylation of Tryptene. Tryptene (0.5 mole), acetic anhydride (1 mole) and phosphoric acid (1 g) were stirred for 25 hours at 20° and then poured onto ice. After the usual processing of the reaction mixture and removal of the unreacted tryptene by distillation, an unsaturated ketone, 2,2-dimethyl-3-methylenehexanone-5, was obtained.

B.p. 162° (745 mm), $n^{20}D$ 1.4530, d_4^{20} 0.8638, MR_D 43.94. $C_9H_{16}O$F. Calculated 43.30.

Absorption maximum of the 2,4-dinitrophenylhydrazone (m.p. 140°) in the UV – 243 mμ (characteristic of allyl ketones [2]).

After standing for six months, the allyl ketone synthesized yielded an equilibrium mixture of ketones, the original one (I) and a vinyl ketone isomeric with it (II), 2,2,3-trimethylhexen-3-one-5. The 2,4-dinitrophenylhydrazone of this mixture of ketones (m.p. 131°) had an absorption maximum in the UV at 352 mμ, which is characteristic of the dinitrophenylhydrazone of a ~50% mixture of vinyl ketone and allyl ketone.

Irradiation of a 50% Mixture of 2,2-Dimethyl-3-methylenehexanone-5 with 2,2,3-Trimethylhexen-3-one-5. The mixture of ketones (0.5 g) with the double bond in different positions was irradiated (mercury lamp PRK-7, current strength 5 A, at a distance of 1 cm) in a quartz tube 0.25 cm in diameter. The irradiation yielded pure 2,2-dimethyl-3-methylenehexanone-5 (I), whose 2,4-dinitrophenylhydrazone had m.p. 140° (from alcohol) and an absorption maximum in the UV at 342 mμ, which is characteristic of allyl ketones [2].

A mixture of the two preparation of ketone (I) melted without depression.

Irradiation of 1-Acetylcyclohexene-1. 1-Acetylcyclohexene-1 was obtained free from the isomeric β,γ-unsaturated ketone by the acylation of cyclohexene at 20° with acetic anhydride in the presence of phosphoric acid: b.p. 201° (754 mm), $n^{20}D$ 1.4887.

The 2,4-dinitrophenylhydrazone melted at 195° (from alcohol) and had an absorption maximum in the UV at 365 mμ (characteristic of pure vinyl ketone [2]).

The 1-acetylcyclohexene-1 was irradiated under the conditions described above. The 2,4-dinitrophenylhydrazone obtained from the irradiation product had m.p. 168° and an absorption maximum in the UV at 355 mμ, which approximately corresponds to a 50% content of 1-acetylcyclohexene-2 in the irradiation product of 1-acetylcyclohexene-1.

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ADDITION OF AMINES TO DIACETYLENE

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Several papers [1-3] have been devoted to investigations of the reaction of diacetylene with nucleophilic reagents. However, as regards the addition of amines to it, there are only brief data without detailed characteristics of the products obtained [1-4].

We established that in benzene solution, even in the cold and in the absence of catalysts, diacetylene added dimethyl- and diethylamines the latter was proved by the infrared spectra. The spectra showed intense frequencies of a conjugated vinylacetylene grouping $-CH=CH-C=CH$ (942, 1610-1620, 2072 and 3288 cm^{-1}).

The amines obtained were colorless oils, which rapidly turned brown on storage. They burned the skin.

1-Dimethylaminobuten-1-yne-3: b.p. 32-34° (5 mm), d_4^{20} 0.8590, $n^{20}D$ 1.5152.

Found %: C 75.91, 76.14; H 9.71, 9.71; N 14.91. C_6H_9N. Calculated %: C 75.75; H 9.53; N 14.72.

1-Diethylaminobuten-1-yne-3: b.p. 53-54° (5 mm), d_4^{20} 0.8556, $n^{20}D$ 1.5208.

Found %: C 78.06, 77.91; H 10.86, 10.77; N 11.43. $C_8H_{13}N$. Calculated %: C 77.99; H 10.64; N 11.37.

The diethylaminobutenyne added the first molecule of bromine in CCl_4 at the triple bond with the formation of a dibromide, whose infrared spectrum had the frequencies of a 1,3-diene grouping (1543 and 1620 cm^{-1}) while the frequencies of a triple bond were practically absent.

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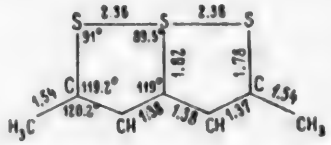
*Original Russian pagination. See C. B. Translation.

ELECTRONIC STRUCTURE OF THIO-THIOPHTHENE

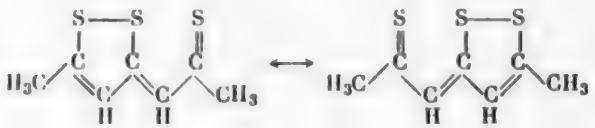
E. M. Shustorovich

Institute of Fine Chemical Technology Moscow

An x-ray structural investigation of the thio-thiophthene molecule was recently published [1]. It was found that this molecule was planar and had the structure and parameters presented below

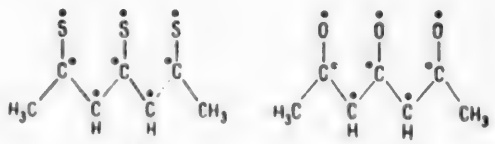


The authors explained the structure and aromatic character of thio-thiophthene by superposition of the structures



This virtually assumes (although the authors did not state this) delocalization of the S — S σ-bond in the general system with the π-electrons of the rings.

It seems more natural to us that in the thio-thiophthene molecule there occurs delocalization of the eight π-electrons in the bicyclic field of eight centers (I).



(I) (II)

Here the S — S bonds are pure π-bonds without σ-bonds analogous to what was proposed by Coulson and Duchesne for the N — N bonds in N_2O_4 [2].

This structure agrees with the fact that the molecule is flat and with the observed values of the angles and interatomic distances. The distance between sulfur atoms equals 2.36 A°, while the length of an ordinary S — S bond (in compounds of the type R — S — S — R) equals 2.04 A° [3]. It may be noted that the N — N distance in N_2O_4, for which a π-bond without a σ-bond has also been proposed, equals ~1.7 A° [3], while in H_2N-NH_2 it equals 1.48 A° [3]. The increase in the X — X distance (X = N, S) is approximately the same (15-16%) in the two cases. The values of the overlap integrals we calculated for these N — N ($2p\pi$) and S — S ($3p\pi$) π-bonds were also approximately the same (~0.08) [4].

In this connection, we may understand why the formation of the oxygen analog of thio-thiophthene (II) must be difficult. In this case the O – O distance remains equal to 2.36 A°, since it is determined by the disposition of the skeleton of carbon atoms and the value of the overlap integral for the $2p\pi$ -orbit of oxygen at this distance must be equal to only 0.004 [4], i.e., a factor of approximately 20 less than for the S – S π -bond.

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DISCUSSION

THE PROBLEM OF A RATIONAL TERMINOLOGY FOR CHELATE FORMATION

V. M. Dziomko

The phenomenon of chelate formation (chelation) and the synthesis of compounds capable of chelate formation has received a great deal of attention in the literature. Meanwhile, no sufficiently suitable term exists for denoting compounds forming chelates. The terms used – "chelate-former", "cyclic complex-former" and "chelating agent" – are either too cumbersome or inconvenient for the Russian language. The term "chelate compound" [1] is also unsatisfactory as many chemists use it to denote metallochelates and not substances capable of chelation. In analogy with the rational terminology of ion exchange [2], it seems advantageous to use the rational term chelant for this purpose.

Process	Agent used for process	Product obtained as a result of process
Absorption	Absorbent	Absorbate
Elution	Eluent	Eluate
Chelation	Chelant	Chelate
Sequestration	Sequestrant	Sequestrate

The term "sequestering agent" [3] is also best replaced by the rational term "sequestrant" [4].

The use of the new term also makes it possible to avoid the inconvenience mentioned above in connection with the use of the term "chelate compound".

LITERATURE CITED

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